Treatment Patterns of Lung Neuroendocrine Tumors (NETs)

Michael S. Broder, MD, MSHS[1]; Eunice Chang, PhD[1]; Beilei Cai, PhD[2]; Maureen P. Neary, PhD[2]; Elya Papoyan, MPH[1]; Al B. Benson III, MD[3]

[1]Partnership for Health Analytic Research, LLC, Beverly Hills, CA 90212; [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ 07936; [3]Northwestern University, Chicago, IL 60611

OBJECTIVE

- Bronchopulmonary or lung NETs represent approximately one-third of primary NETs, a broad set of rare, often slow growing tumors.[1]
- U.S. incidence of primary NETs has increased from 10.9 cases per million person years (PMPY) in 1973 to 69.8 PMPY in 2012. Lung NET incidence rose from 3.0 to 16.0 cases PMPY.[2]
- Surgery may be curative early, and isolated liver metastasis may be resected.
- Otherwise, treatment includes pharmacologic therapy with agents typically used in other NET (e.g., everolimus, sunitinib, somatostatin analogues) or in small cell lung cancer (SCLC) (e.g., cisplatin/etoposide).[3*]
- The objective of this study is to describe the real-world treatment patterns of lung NET patients.

* At the time of this study, lung NET was included in both the SCLC and NET NCCN guidelines. In the most recent version of the NCCN guidelines (Version 3.2017), lung NET has been removed from the SCLC guidelines.

METHODS

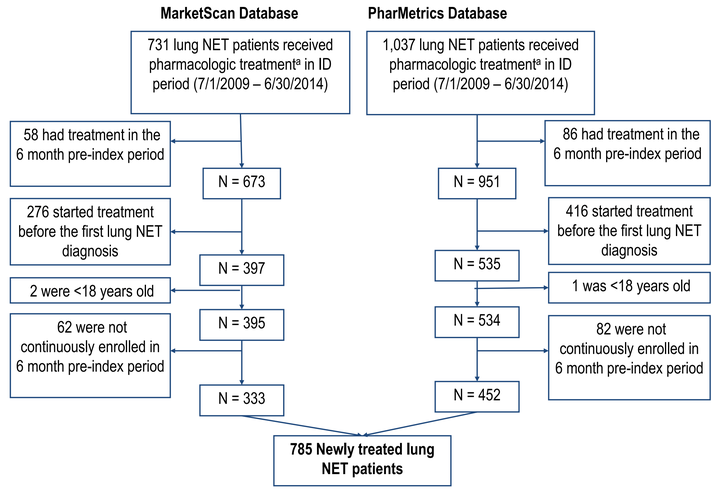
- Retrospective cohort study using 2009-2014 data from 2 US claims databases: Truven Health Analytics MarketScan and IMS PharMetrics.
  - Inclusion Criteria:
    - Age ≥18 years
    - ≥1 inpatient or ≥2 outpatient claims for lung NET (ICD-9-CM 209.21, 209.61) within the study ID period 7/1/2009-6/30/2014
    - Evidence of pharmacologic treatments after the first lung NET diagnosis
  - Exclusion Criteria:
    - Lack of at least six months' enrollment before the index date (baseline) with no prior treatment
- Variable follow up: until end of enrollment or 12/31/14, whichever occurred first.
- Outcome measures included:
  - Pharmacotherapy:
    - Cytotoxic chemotherapies (CC) – carboplatin, cisplatin, etoposide, temozolomide, streptozocin, doxorubicin, liposomal doxorubicin, fluorouracil, capecitabine, dacarbazine, oxaliplatin, and thalidomide
    - Somatostatin analogues (SSA) – octreotide SA, octreotide LAR, and lanreotide
    - Targeted therapies (TT) – everolimus, and sunitinib – and interferon (IF)
  - Liver directed therapy (i.e., liver surgery excluding transplant, liver transplant, liver lesion ablation, embolization, radiation therapy)
- First-line therapy defined as the treatment regimen observed on or within 90 days of the index date.
- Second-line therapy defined as switch from one category of pharmacotherapy to another (e.g., from SSA alone to CC alone), or the addition of a new category of treatment (e.g., from SSA alone to SSA plus CC).
- Statistical Analysis:
  - Kaplan-Meier failure plot and graphical analyses using GRAPHx™, which uses multi-colored line segments to represent various treatments and plots them over time.

RESULTS

- 785 newly pharmacologically treated lung NET patients were identified (Figure 1).
  - Mean (SD) age of 58.6 (9.1) years, 54.0% female, and 52.5% of the patients between 55 and 64 years (Table 1).
- 78.2% started first-line therapy with CC, 18.1% with SSA, and 1.1% received TT (Table 2).
- Mean duration of first-line therapy was 397 days for SSAs, 142 for CC, 135 for TT.
  - Half of the patients discontinued first-line treatment SSA by 460 days (1.26 years) of treatment, and CC by 102 days (0.28 years) (Figure 2).
- 74.1% of patients discontinued first-line therapy with no subsequent pharmaceutical or liver directed therapy; 7.6% (60/785) used second-line regimens (Table 2). Most (74%) CC users observed to use 2nd line therapy switched to SSA alone or SSA combination.
  - 61% (14/23) SSA users observed to use 2nd line switched to an SSA combination.
- No clear pattern was visible following first-line therapy, although many chemotherapy-treated patients appeared to have liver-directed therapy around or after chemotherapy (Figure 3).

RESULTS (continued)

Figure 1. Patient Identification



[a] SSA, CC, TT, and IF.

Table 1. Patient Demographics and Follow-up, Stratified by First-Line Pharmacologic Treatment

	First-Line Treatment								
	CC	SSA[a]	TT	SSA+ CC	SSA+TT	TT+CC	SSA+IF	SSA+ TT+ CC	All
N	614	142	9	9	6	2	2	1	785
%	78.2	18.1	1.1	1.1	0.8	0.3	0.3	0.1	100.0
Age, years, mean (SD)	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 (0.0)	58.6 (9.1)
Female, n (%)	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)
Follow-up[b], days, mean (SD)	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)

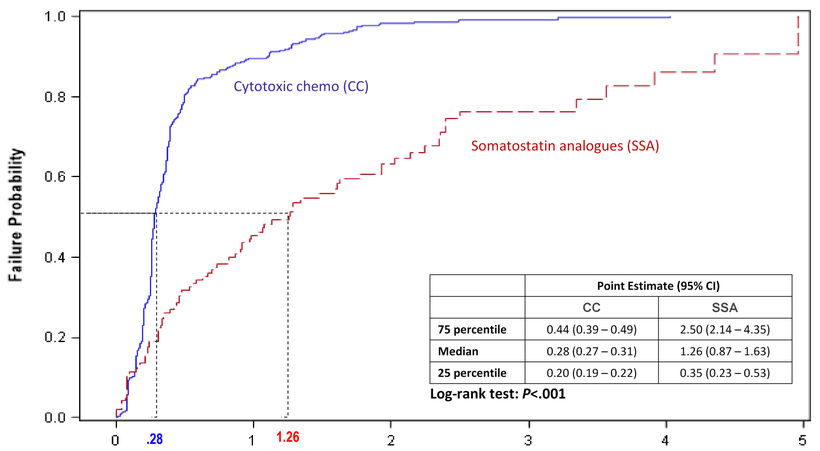
[a] 97 with octreotide LAR, 45 with octreotide SA, and 0 with lanreotide.
[b] From index date until study end or end of enrollment (whichever occurred first) regardless of treatment continuation. Treatment duration is shown in Table 2, below.

Table 2. Use of First-Line Pharmacologic Treatment, Stratified by First-Line Treatment

	First-Line Treatment								
	CC	SSA	TT	SSA+CC	SSA+ TT	TT+ CC	SSA+ IF	SSA+TT+ CC	All
N	614	142	9	9	6	2	2	1	785
%	78.2	18.1	1.1	1.1	0.8	0.3	0.3	0.1	100.0
First-line treatment duration, days, mean (SD)	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[a], n (%)									
Stop	505 (82.2)	64 (45.1)	7 (77.8)	3 (33.3)	1 (16.7)	1 (50.0)	0 (0.0)	1 (100.0)	582 (74.1)
Switch	31 (5.0)	23 (16.2)	1 (11.1)	3 (33.3)	1 (16.7)	0 (0.0)	1 (50.0)	0 (0.0)	60 (7.6)
End of enrollment	78 (12.7)	55 (38.7)	1 (11.1)	3 (33.3)	4 (66.7)	1 (50.0)	1 (50.0)	0 (0.0)	143 (18.2)

[a] Stop = first-line treatment termination observed during the follow-up period; no second-line pharmacologic therapy observed; Switch = first-line treatment termination observed during the follow-up period; second-line pharmacologic therapy (switch or addition) observed; End of enrollment = at the end of enrollment, first-line treatment was still ongoing.

Figure 2. Time to Discontinue First-Line Treatment in Patients Initiating Cytotoxic Chemotherapy or Somatostatin Analogues[a]

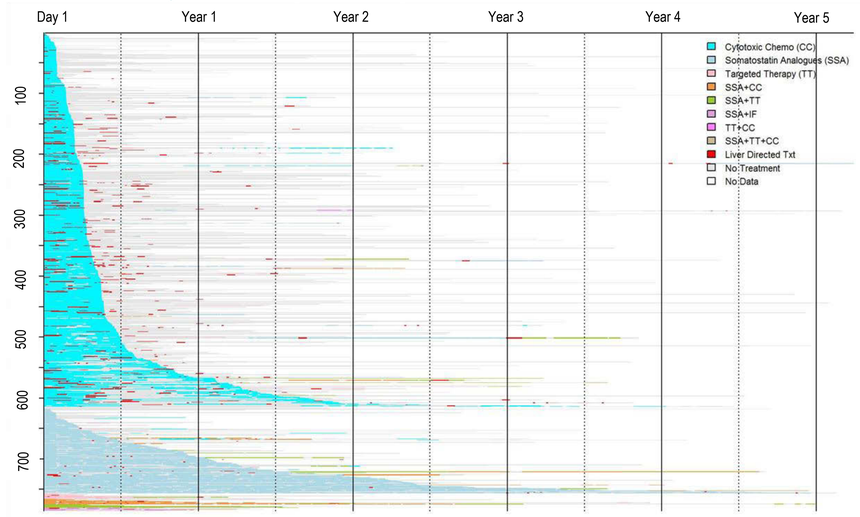


	No. of Patients at Risk										
	Index Date	0.5Y	1Y	1.5Y	2Y	2.5Y	3Y	3.5Y	4Y	4.5Y	5Y
CC	614	104	48	18	5	2	3	1	1	0	0
SSA	142	84	59	36	27	13	9	6	4	2	0

[a] 9 patients treated with TT first-line not shown.

RESULTS (continued)

Figure 3. Comprehensive Graphical Representation of Pharmacologic Treatment for 785 Patients with Lung NET



Day 1: First date of pharmacologic treatment

LIMITATIONS

- Claims are designed for payment, not research; codes may be used incorrectly.
- Reason for discontinuation is not reported in claims nor are deaths. So, although therapy may be stopped when patients are terminally ill, this cannot be confirmed.
- Treating NETs is complex and treatments are individualized based on many factors (e.g., tumor size, pathology, etc.) not available in our database.
- Results may not be applicable to non-commercially insured individuals.

CONCLUSIONS

- This study combined two very large, nationally representative claims databases (representing >100 million covered lives) to describe real-world treatment patterns for lung NETs in the US.
- Over 75% of patients began therapy with chemotherapy and almost 20% with somatostatin analogue monotherapy.
- The high proportion of chemotherapy use and low proportion receiving second-line treatment seems consistent with NCCN SCLC (rather than NET) treatment guidelines. For typical lung NETs, the NET guidelines mention chemotherapy (Category 3*) 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).[1,4-7]
  - Lung NET patients treated with chemotherapy may have had more aggressive tumor histology, but this cannot be confirmed in our dataset, nor could we verify if SCLC patients were miscoded as having lung NET.
- Lung NET patients used first-line SSA treatment for a median of more than one year compared to just over 3 months for chemotherapy.
- The majority of patients stopped treatment while still enrolled in the health plan, although if patients had secondary insurance we might have missed further treatment.
- 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.

* Category 3: major NCCN disagreement that the intervention is appropriate.

REFERENCES

1. NCCN. Neuroendocrine Tumors. National Comprehensive Cancer Network; 2017.
2. Dasari A, Shen C, Halperin D, et al. Changing Trends in the Incidence, Prevalence and Survival of Neuroendocrine Tumors in the United States: A SEER Population-Based Study of 34,971 Cases. *JAMA Oncol.* In press.
3. NCCN. Small Cell Lung Cancer. National Comprehensive Cancer Network; 2016.
4. NCCN. Neuroendocrine Tumors. National Comprehensive Cancer Network; 2011.
5. NCCN. Neuroendocrine Tumors. National Comprehensive Cancer Network; 2013.
6. NCCN. Neuroendocrine Tumors. National Comprehensive Cancer Network; 2014.
7. NCCN. Neuroendocrine Tumors. National Comprehensive Cancer Network; 2016.

2017 Multidisciplinary Thoracic Cancers Symposium
March 16-18, 2017 | San Francisco, CA, USA

Scan this QR code
OR Visit the web at:
http://novartis.medicalcongresspos ters.com/Default.aspx?doc=6d37b

OR Text: Q6d37b To:8NOVA (86682) US Only
+18324604729 North, Central and South Americas; Caribbean; China
+447860024038 UK, Europe & Russia
+46737494608 Sweden, Europe

Research was conducted by Partnership for Health Analytic Research, LLC.
This study was sponsored by Novartis Pharmaceuticals Corporation.