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Treatment Patterns of Gastrointestinal (GI) Neuroendocrine Tumors (NETs)

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BACKGROUND

- Neuroendocrine tumors (NET) comprise a broad set of rare tumors, approximately 2/3 of which occur in the gastrointestinal tract.[1]
- Surgery may be curative in the early stages, but delayed diagnosis is typical.
- NCCN guidelines for unresectable and metastatic GI NET recommend somatostatin analogues (SSA) as first-line treatment, but do not recommend a particular treatment sequence for the remaining therapies.[2]
- To date, there have been no studies using large claim databases to assess real-world treatment patterns of GI NET.

OBJECTIVE

- To describe the current real-world treatment patterns of GI NET in a large sample of patients from two commercial claims databases.

METHODS

- Retrospective, cross-sectional study using 2009-2014 data from 2 U.S. commercial claims databases: Truven Health Analytics MarketScan and IMS PharMetrics.
- Study population
  - Inclusion Criteria:
    - Age ≥ 18
    - ≥ 1 inpatient or ≥ 2 outpatient claims for GI NET (benign or malignant) within the study period (1/1/2009-12/31/2014)
    - Evidence of pharmacologic treatment within the ID period (7/1/2009-6/30/2014)
      - The first GI NET pharmacologic treatment claim on or after the appearance of the first GI NET diagnosis code was considered the index date.
  - Exclusion Criteria:
    - lack of at least six months enrollment before the index date (baseline)
    - evidence of pharmacologic treatment during the baseline period
- Variable follow up: until end of enrollment or 12/31/14, whichever came first.
- Therapies considered:
  - Pharmacotherapy: somatostatin analogues (SSA), targeted therapies (TT), cytotoxic chemotherapies (CC) and interferon (IF).
  - Liver directed therapy: liver resection, transplant, lesion ablation, embolization, and radiation therapy.
- First-line therapy: the first pharmacologic treatment regimen observed on or within 90 days following the index date.
- Second-line therapy: 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:
  - Means and proportions presented in tabular analyses
  - Kaplan-Meier failure plot to show duration of first-line therapy
- Graphical analyses using GRAPHx™

RESULTS

- 2,258 newly treated GI NET patients were identified **(Figure 1)**.
- 59.6% started first line therapy with SSA monotherapy, 33.3% CC, 3.6% TT, and 0.1% IF.
  - 75 patients (3.3%) received SSA in combination with either CC, TT, and/or IF.
- Mean duration of first-line therapy was 361 days overall (449 days for SSA, 215 for CC, 267 for TT) **(Table 1)**.
- Only 8.4% (n=189) of patients started second-line therapy **(Table 1)**.
  - Most common second line was combination therapy with SSA (i.e., CC or TT added).
  - In patients without first-line SSA, most received second line SSA.
- 58.9% of patients had no subsequent pharmacologic treatment after first-line therapy **(Table 1)**.
  - Patients were still enrolled but no longer had claims for pharmacologic treatment till the end of study period.
  - Identified as the colored line segments that terminate in gray segments of variable length **(Figure 3)**.
- There was no clear pattern visible after first-line therapy **(Table 2, Figure 3)**.
  - Liver directed therapy appears dispersed throughout periods of both pharmacologic treatment and periods of no pharmacologic treatment.

Figure 1. Patient Identification

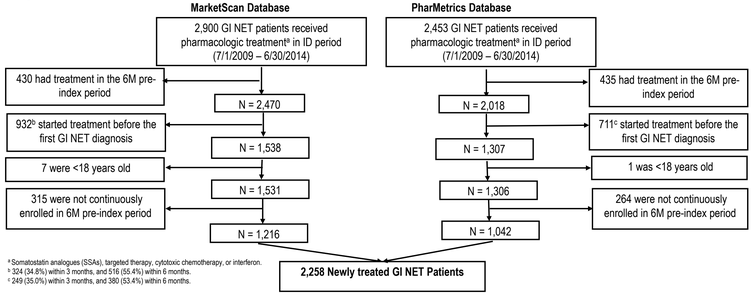

Table 1. Patient Demographics & Use of First-Line Treatments, Stratified by First-Line Treatment

	First-Line Treatment									All Newly Treated Patients
	SSA	CC	TT	SSA+CC	SSA+TT	TT+CC	IF	SSA+IF	SSA+TT+CC	
N (%)	1,345[a] (59.6)	752 (33.3)	81 (3.6)	42 (1.9)	31 (1.4)	3 (0.1)	2 (0.1)	1 (0.0)	1 (0.0)	2,258 (100.0)
Age, year, mean (SD)	56.3 (9.5)	54.7 (9.9)	54.9 (10.5)	53.5 (10.9)	53.8 (10.1)	59.3 (3.8)	58.5 (3.5)	58.0 (n/a)	55.0 (n/a)	55.6 (9.7)
Female, no. (%)	677 (50.3)	341 (45.3)	40 (49.4)	26 (61.9)	17 (54.8)	1 (33.3)	1 (50.0)	0 (0.0)	0 (0.0)	1,103 (48.8)
Region, no. (%)										
Midwest	321 (23.9)	183 (24.3)	20 (24.7)	13 (31.0)	7 (22.6)	0 (0)	1 (50.0)	0 (0)	0 (0)	545 (24.1)
Northeast	261 (19.4)	150 (19.9)	12 (14.8)	11 (26.2)	7 (22.6)	1 (33.3)	0 (0)	0 (0)	0 (0)	442 (19.6)
South	563 (41.9)	323 (43.0)	36 (44.4)	12 (28.6)	15 (48.4)	2 (66.7)	1 (50.0)	0 (0)	1 (100.0)	953 (42.2)
West	200 (14.9)	96 (12.8)	13 (16.0)	6 (14.3)	2 (6.5)	0 (0)	0 (0)	1 (100.0)	0 (0)	318 (14.1)
Days of follow-up, mean (SD) [median]	621 (468.5) [500]	514 (409.1) [393]	454 (403.6) [290]	588 (424.1) [455]	425 (269.6) [360]	244 (140.7) [216]	675 (145.7) [675]	836 (n/a) [836]	496 (n/a) [496]	576 (447.1) [454]
Duration of first-line treatment, days, mean (SD)	449 (434.2)	215 (228.8)	267 (325.7)	408 (327.9)	276 (189.5)	208 (165.6)	251 (285.0)	836 (0)	426 (0)	361 (385.0)
First-line ending status, no. (%)										
Stop	635 (47.2)	609 (81.0)	44 (54.3)	26 (61.9)	14 (45.2)	1 (33.3)	1 (50.0)	0 (0)	1 (100.0)	1,331 (58.9)
Switch	128 (9.5)	33 (4.4)	14 (17.3)	5 (11.9)	7 (22.6)	1 (33.3)	1 (50.0)	0 (0)	0 (0)	189 (8.4)
End of enrollment	582 (43.3)	110 (14.6)	23 (28.4)	11 (26.2)	10 (32.3)	1 (33.3)	0 (0)	1 (100.0)	0 (0)	738 (32.7)

[a] 964 with octreotide LAR, 380 with octreotide SA, and 1 with lanreotide.

Table 2. Second-Line Treatment, Stratified by First-Line Treatment

	First-Line Treatment							All Newly Treated Patients
	SSA	CC	TT	SSA+CC	SSA+TT	TT+CC	IF	
N (%)	128 (67.7)	33 (17.5)	14 (7.4)	5 (2.6)	7 (3.7)	1 (0.5)	1 (0.5)	189 (100.0)
Second-line treatment, no. (%)								
SSA+TT	51 (39.8)	4 (12.1)	4 (28.6)	3 (60.0)		0 (0)	1 (100.0)	63 (33.3)
SSA+CC	33 (25.8)	6 (18.2)	0 (0)		5 (71.4)	0 (0)	0 (0)	44 (23.3)
CC	24 (18.8)		4 (28.6)	0 (0)	1 (14.3)	0 (0)	0 (0)	29 (15.3)
SSA		16 (48.5)	5 (35.7)	0 (0)	0 (0)	1 (100.0)	0 (0)	22 (11.6)
TT	12 (9.4)	7 (21.2)		2 (40.0)	0 (0)	0 (0)	0 (0)	21 (11.1)
SSA+IF	3 (2.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1.6)
IF	2 (1.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		2 (1.1)
TT+CC	1 (0.8)	0 (0)	1 (7.1)	0 (0)	0 (0)		0 (0)	2 (1.1)
SSA+TT+CC	1 (0.8)	0 (0)	0 (0)	0 (0)	1 (14.3)	0 (0)	0 (0)	2 (1.1)
SSA+CC+IF	1 (0.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.5)

Figure 2. Time to Discontinuation of First-Line Treatment

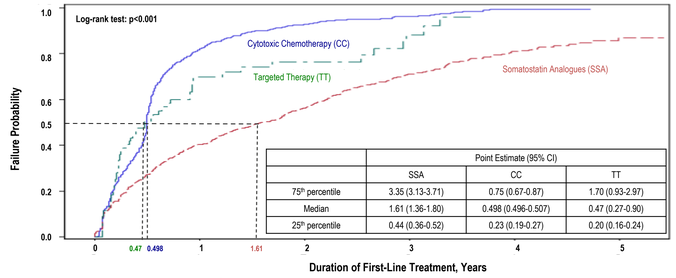

Figure 3. Treatment Patterns GRAPHx™

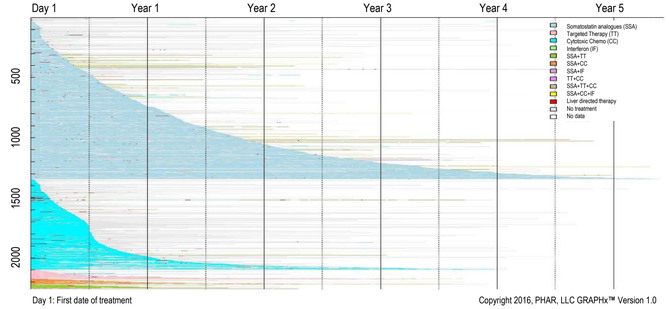

Figure 3 shows a graphical representation of first-line therapy initiation, duration of use, and switching to subsequent therapy among individual patients. The majority of patients initiated treatment with SSA monotherapy and there are no clear patterns visible after first-line therapy. Periods of enrollment without therapy appear as gray segments and liver directed therapy appear as red dots dispersed throughout.

LIMITATIONS

- Results reflect only patients with commercial insurance and not those with Medicaid, Medicare or no insurance
- Patients, therapies and procedures were identified using ICD-9-CM diagnosis codes, NDC codes, ICD-9 codes, and CPT procedure codes; pathologic diagnosis were not available, and misclassification may have occurred.
- Misclassification of ongoing patients as newly treated may have occurred if there were treatment gaps of > 6 months.
- Less than 10% of patients were observed to initiate second-line treatment, so conclusions about treatment patterns are based on limited information.
  - Median enrollment of less than 2 years likely prevented us from observing second-line treatment in many patients
- Data are from 2009-2014 and patterns may have changed since then due to newly approved agents for GI NET.

CONCLUSIONS

- More than half of pharmacologically treated patients began treatment with SSAs, which appears to have been well-tolerated based on average duration of use over 18 months (1.61 years).
- One-third of patients began therapy with chemotherapy, which is recommended by NCCN guidelines only if no other options are feasible.
- Despite the many available treatment options, more than half of patients had no subsequent pharmacological treatments after discontinuing first-line therapy despite continued enrollment in health plan.
- Studies directed at verifying these results are warranted; ideally these studies will be performed using clinically detailed information from medical charts.

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