Clinical Characteristics, Treatment Patterns, and Health Care Resource Utilization in Unresectable, Locally Advanced, Stage III Non-Small Cell Lung Cancer: A Medical Record Review Study in the United States and Canada

Samantha K. Kurosky,[1] Alyssa B. Klein,[2] Rohan Parikh,[1] Laurel Trantham,[1] Yiduo Zhang,[2] Christina Levine,[1] James A. Kaye[3]

[1]RTI Health Solutions, Research Triangle Park, NC, USA; [2]AstraZeneca, Gaithersburg, MD, USA; [3]RTI Health Solutions, Waltham, MA, USA

PCN239

INTRODUCTION

- In 2012, lung cancer was diagnosed in an estimated 240,000 patients and caused 185,000 deaths in North America.[1] Approximately 90% of lung cancers are non-small cell lung cancer (NSCLC)[2] and nearly one-third are initially diagnosed at stage III.[3] Among stage III tumors, 30% to 50% are locally advanced and inoperable with a poor prognosis.[4,5]
- Treatment for unresectable stage III NSCLC typically consists of definitive platinum-based chemotherapy given concurrently with radiotherapy (i.e., concurrent chemoradiation).[6] Median progression-free survival following chemoradiation is approximately 8 months, and 5-year survival is only 15%.[7,8]
- Due to the poor prognosis associated with unresectable stage III NSCLC and the limited effectiveness of standard care, there remains a need for treatment options that are effective and sustain quality of life. Further research on real-world treatment, outcomes, and health care resource burden in these populations may provide needed data for assessing unmet treatment need and current information for comparing the impact of future novel therapies for treating NSCLC.

OBJECTIVE

- To describe real-world clinical characteristics, treatment patterns, and health care resource utilization in patients who did not experience disease progression during receipt of their first two cycles of chemoradiation for unresectable stage III NSCLC in the United States (US) and Canada.

METHODS

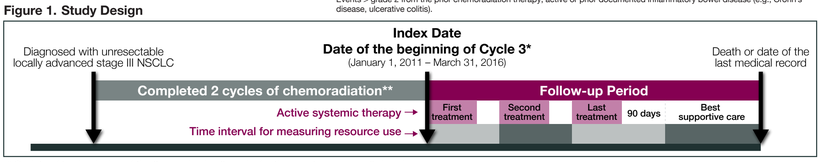
- We conducted a retrospective review of medical records of patients diagnosed with unresectable, locally advanced, stage III NSCLC in the US and Canada.
- A convenience sample of oncologists selected a quasi-random sample of patients from their practice and abstracted anonymized, retrospective data from the patients' medical records.
- The sample consisted of 57 physicians in the US and 13 in Canada, geographically dispersed across their respective countries.
- Patient selection criteria are listed in Table 1.
- The start date of the third cycle or 3 weeks following the end of the second cycle defined the index date (Figure 1).
- This is a preliminary analysis of a subset of patients with cleaned data.

Table 1. Patient Selection Criteria

Inclusion Criteria	Exclusion Criteria
• Confirmed diagnosis of unresectable, locally advanced, stage III NSCLC • Completed at least two cycles of platinum-based chemotherapy concurrent with radiation therapy and did not experience disease progression during these two cycles – For patients who received a third cycle, they must have started the third cycle between January 1, 2011, and March 31, 2016 – For patients who did not receive a third cycle, the start date of the second cycle plus 3 weeks must fall between January 1, 2011, and March 31, 2016 – Aged 18 years or older at the beginning of the third cycle (for those receiving a third cycle) or the beginning of the second cycle plus 3 weeks (for those not receiving a third cycle)	• Evidence of other malignant neoplasms (except nonmelanoma skin cancer or carcinoma in situ) • Mixed small cell and non-small cell histology or not otherwise specified histology • Participation in a clinical trial related to treatment of locally advanced NSCLC • Patients with evidence of certain other treatments/ conditions were excluded[a]

[a] Included brain metastases or spinal cord compression unless asymptomatic or treated and stable (not requiring steroids); exposure to immunomodulatory therapy at any point in time; active or prior documented autoimmune or inflammatory disorder; prior exposure to any anti–PD-L or PD-L1 antibody; severe or uncontrolled systemic diseases, including active bleeding diatheses or active infections including hepatitis B and C and HIV; uncontrolled illness such as symptomatic congestive heart failure, uncontrolled hypertension, or unstable angina pectoris; any unresolved toxicity Common Terminology Criteria for Adverse Events > grade 2 from the prior chemoradiation therapy; active or prior documented inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis).

Figure 1. Study Design



* Or date of the beginning of the 2nd cycle plus 3 weeks for those not receiving a 3rd cycle.
** Patient did not experience disease progression during this period.

RESULTS

Patient Demographics, Clinical Characteristics, and Follow-Up

- Among 135 patients in the US and 39 patients in Canada, 68.2% (US) and 69.2% (Canada) were male; 71.9% (US) and 84.6% (Canada) were white (Table 2).
- Only 15.6% (US) and 7.7% (Canada) and received PD-L1 testing at initial diagnosis (Table 2).
- The mean (standard deviation [SD]) age in years at the index date was 62.2 (8.7) (US) and 60.8 (8.2) (Canada) years (Table 2).
- Among patients initially diagnosed prior to diagnosis of unresectable stage III NSCLC (US, 23.7%; Canada, 46.2%), 53.1% in the US and 61.1% in Canada received prior NSCLC-directed treatment.
- The median duration of observable follow-up was 20.7 months in the US and 21.6 months in Canada.

Concurrent Chemoradiation

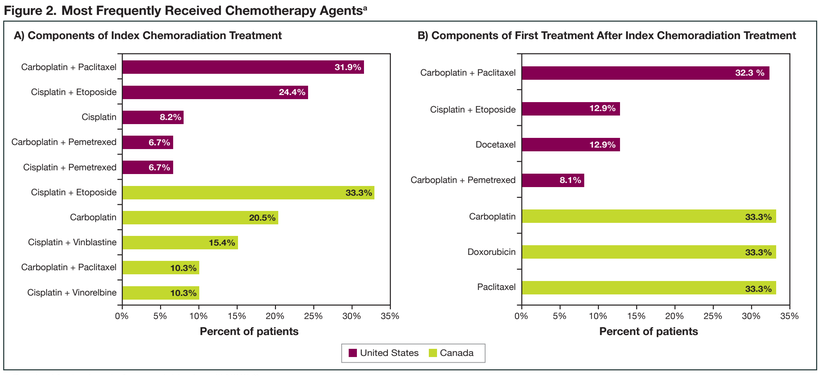
- The mean (SD) duration of the index chemoradiation treatment was 2.1 (1.5) months in the US and 2.9 (2.1) months in Canada. The median number of cycles administered was two in the US and three in Canada (Table 3).
  - The index chemoradiation treatment included the first two cycles required for all patients to enter the study.
- At the start of the index chemoradiation treatment, 85.9% of patients in the US and 56.4% of patients in Canada had a performance status of 0 or 1 (Table 3).
- In the US, the most frequently administered chemotherapies were carboplatin and paclitaxel (31.9%) and cisplatin and etoposide (24.4%). In Canada, the most frequently administered chemotherapies were cisplatin and etoposide (33.3%) and carboplatin (20.5%) (Figure 2).
  - The majority of patients received the index chemoradiation in accordance with National Comprehensive Cancer Network guidelines (US, 95.6%; Canada, 94.9%).
- In the US, 75.6% of patients stopped the index chemoradiation treatment due to completion of the planned course of treatment. In Canada, 64.1% stopped due to this reason, and 23.1% stopped due to progressive disease (Table 3).

Table 2. Sample Characteristics

Characteristic	US		Canada	
Number of patients (N, %)	135	100%	39	100%
Male (n, %)	92	68.2%	27	69.2%
White (n, %)	97	71.9%	33	84.6%
Age at index date, years (mean, SD)	62.2	8.7	60.8	8.8
Median	62.7		60.7	
Stage at initial diagnosis (n, %)				
Stage IIB	4	3.0%	2	5.1%
Stage IIIA	72	53.3%	23	59.0%
Stage IIIB	58	43.0%	14	35.9%
Don't know	1	0.7%	0	0.0%
Tumor histology (n, %)				
Adenocarcinoma	97	71.9%	19	48.7%
Large cell carcinoma	3	2.2%	6	15.4%
Squamous cell carcinoma	35	25.9%	12	30.8%
Don't know	0	0.0%	2	5.1%
Tumor grade at initial diagnosis (n, %)[a]				
Grade 1	14	10.4%	4	10.3%
Grade 2	63	46.7%	16	41.0%
Grade 3	37	27.4%	16	41.0%
Grade 4	2	1.5%	3	7.7%
Could not be assessed/don't know	19	14.1%	0	0.0%
PD-L1 testing at initial diagnosis (n, %)				
Yes	21	15.6%	3	7.7%
Met test threshold for PD-L1 expression among tested	10	47.6%	2	66.7%
No	113	83.7%	35	89.7%
Don't know	1	0.7%	1	2.6%
Performance status of 0 or 1 at index date (n, %)	120	88.9%	20	51.3%
Charlson Comorbidity Index score (mean, SD)[b]	1.6	1.7	1.3	1.3
Smoking status				
Current smoker	33	24.4%	13	33.3%
Former smoker	87	64.4%	24	61.5%
Nonsmoker	14	10.4%	2	5.1%
Don't know	1	0.7%	0	0.0%

[a] Edge and Compton, 2010.[9]
[b] Calculation does not include cancer as a comorbidity.

Figure 2. Most Frequently Received Chemotherapy Agents[a]



[a] Received for treatment of unresectable stage III NSCLC.

Table 3. Treatment Characteristics

Characteristic	US				Canada			
	Index Chemoradiation		First Treatment After Chemoradiation		Index Chemoradiation		First Treatment After Chemoradiation	
Total patients initiating treatment (N, %)	135	100%	63	100%	39	100%	5	100%
Total patients discontinuing treatment (n, %)	135	100%	63	100%	39	100%	5	100%
Chemoradiation (n, %)	135	100%	10	15.9%	39	100%	1	20.0%
Duration in months (mean, SD)[a]	2.1	1.5	1.1	0.7	2.9	2.1	4.8	
Chemotherapy only (n, %)	0	0.0%	52	82.5%	0	0.0%	2	40.0%
Duration in months (mean, SD)[a]	–	–	2.3	2.0	–	–	2.7	1.5
Radiotherapy only (n, %)	0	0.0%	1	1.6%	0	0.0%	2	40.0%
Duration in months (mean, SD)[a]	–	–	0.2	–	–	–	1.0	1
Performance status of 0 or 1 at start of treatment	116	85.9%	53	84.1%	22	56.4%	1	20.0%
Number of cycles (median)	2.0		3.0		3.0		3.0	
Reason for stopping treatment[a,b]								
Adverse event	2	1.5%	3	4.8%	1	2.6%	1	20.0%
Patient decision	21	15.6%	11	17.5%	4	10.3%	1	20.0%
Progressive disease	9	6.7%	14	22.2%	9	23.1%	3	60.0%
Completion of planned course of treatment	102	75.6%	37	58.7%	25	64.1%	0	0.0%
Loss to follow-up	2	1.5%	0	0.0%	0	0.0%	0	0.0%
Death	0	0.0%	0	0.0%	1	2.6%	0	0.0%
Other	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Don't know	3	2.2%	3	4.8%	0	0.0%	0	0.0%

[a] Among patients who discontinued treatment during their available follow-up.
[b] A patient could have had more than one reason for stopping treatment.

Additional Treatment for Unresectable Locally Advanced, Stage III NSCLC

- In the US, 46.7% of patients received additional treatment for stage III disease after the index chemoradiation. Among these patients, 82.5% received chemotherapy alone, 15.9% received additional chemoradiation, and 1.6% received radiotherapy alone. In Canada, 12.8% of patients received additional treatment. Among them, 40.0% received chemotherapy alone, and 20.0% received additional chemoradiation. In both countries, patients who received chemotherapy (alone or with radiation) received a median of three cycles (Table 3).
- The most frequently received chemotherapies after initial chemoradiation in the US were carboplatin with paclitaxel (32.3%), cisplatin with etoposide (12.9%), and docetaxel (12.9%). In Canada, patients most commonly received single-agent carboplatin, doxorubicin, or paclitaxel (33.3% each) (Figure 2).
- In the US, 58.7% of patients stopped the first treatment after chemoradiation due to completion of the planned treatment course, while 22.2% stopped due to disease progression. In Canada, 60.0% stopped due to progressive disease (Table 3).

Treatment for Metastatic Disease

- Thirty-eight patients in the US and 19 patients in Canada developed distant metastases during their available follow-up period.
- Of these patients, 39.5% (US) and 52.6% (Canada) received chemotherapy, 26.3% (US and Canada, each) received biologics, and 18.4% (US) and 5.3% (Canada) received other targeted therapies for treatment of metastatic NSCLC.
- During available follow-up, 70.0% (US) and 80.0% (Canada) received only one line of systemic therapy for metastatic disease; the remaining received two or more lines. Only 30.0% (US) and 6.7% (Canada) received maintenance therapy.

Health Care Resource Utilization

- During the index chemoradiation treatment, 77.0% (US) and 74.4% (Canada) of patients had health care utilization information documented in their medical record. Among them, patients had a monthly median of 1.4 (US) and 0.8 (Canada) NSCLC-related visits.
- During the first treatment after chemoradiation, 74.6% (US) and 20.0% (Canada) of patients had documented utilization with a monthly median of 1.7 (US) and 1.1 (Canada) NSCLC-related visits.

CONCLUSIONS

- In this study, patients treated with concurrent chemoradiation generally initiated treatment according to guidelines.
- In the US and Canada, most patients completed definitive chemoradiation therapy as planned. However, a substantial proportion of patients receive subsequent treatment until experiencing disease progression, particularly in Canada.
- PD-L1 testing was uncommon at the index date. Given the high level of expression in patients that were tested, testing for PD-L1 expression in earlier stages may assist in identifying patients who may benefit from novel immuno-oncology therapies.

References

1. Ferlay J, Soerjamataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-86.
2. Govindan R, Page N, Morgensztern D, et al. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. J Clin Oncol. 2006;24:4539-44.
3. Morgensztern D, Ng SH, Gao F, et al. Trends in stage distribution for patients with non-small cell lung cancer: a National Cancer Database survey. J Thorac Oncol. 2010 Jan;5(1):29-33.
4. Mauguen A, Le Péchoux C, Saunders MI, et al. Hyperfractionated or accelerated radiotherapy in lung cancer: an individual patient data meta-analysis. J Clin Oncol. 2012 Aug 1;30(22):2788-97.
5. Siegel R, DeSantis C, Virgo K, et al. Cancer treatment and survivorship statistics, 2012. CA Cancer J Clin. 2012 Jul-Aug;62(4):220-41.
6. Ettinger DS, Wood DE, Aisner DL, et al. Non–small cell lung cancer, version 5.2017, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2017 Apr;15(4):504-35.
7. Ahn JS, Ahn YC, Kim JH, et al. Multinational Randomized phase III trial with or without consolidation chemotherapy using docetaxel and cisplatin after concurrent chemoradiation in inoperable stage III non-small-cell lung cancer: KCSG-LU05-04. J Clin Oncol. 2015 Aug 20;33(24):2660-6.
8. Aupérin A, Le Péchoux C, Rolland E, et al. Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer. J Clin Oncol. 2010 May 1;28(13):2181-90.
9. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol. 2010 Jun;17(6):1471-4.

Contact Information

Alyssa B. Klein, MPH
Associate Director, Epidemiology – IO Lung
AstraZeneca
Phone: +1.301.398.2135
E-mail: alyssa.klein@astrazeneca.com

Presented at the ISPOR 23rd Annual International Meeting, May 19-23, 2018, Baltimore, Maryland, USA