Unresectable, Locally Advanced, Stage III Non-Small Cell Lung Cancer: Real-World Clinical Characteristics, Treatment Patterns, and Health Care Resource Utilization in Europe

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INTRODUCTION

- In Europe in 2012, lung cancer was diagnosed in more than 400,000 patients and caused nearly 350,000 deaths.[1] Most lung cancers are non-small cell lung cancer (NSCLC)[2] and approximately one-third are at stage III at initial diagnosis.[3] Between 30% and 50% of stage III cancers are inoperable.[4,5]
- Patients with unresectable stage III NSCLC typically receive definitive platinum-based chemotherapy given concurrently with radiotherapy (i.e., concurrent chemoradiation).[6] Following chemoradiation, median progression-free survival is an estimated 8 months, and 5-year survival is 15%.[7,8]
- Poor prognosis associated with unresectable stage III NSCLC and the limited effectiveness of standard care indicate a continued need for effective treatment options. Research on real-world treatment, outcomes, and health care resource burden associated with unresectable stage III NSCLC may provide needed data for assessing unmet treatment needs and current information for evaluating 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 in the United Kingdom (UK), Germany, and Spain who did not experience disease progression during receipt of their first two cycles of chemoradiation for unresectable stage III NSCLC.

METHODS

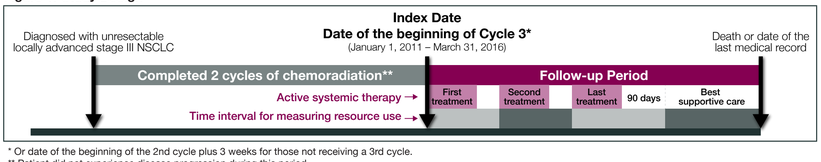
- We conducted a retrospective medical record review of patients treated with at least two cycles of concurrent chemoradiation for unresectable, locally advanced, stage III NSCLC in the UK, Germany, and Spain.
- A convenience sample of oncologists selected a quasi-random sample of patients from their practice and abstracted anonymized, retrospective data from the patients' medical records.
- The sample consisted of 45 physicians in the UK, 94 in Germany, and 45 in Spain, geographically dispersed across their respective countries. Patient selection criteria are listed in Table 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 162 patients in the UK, 155 patients in Germany, and 159 patients in Spain, 64.8% to 78.6% were male and 89.5% to 98.7% were white (Table 2).
- In each country, between 82.7% and 94.3% of patients were not tested for PD-L1 expression at initial diagnosis (Table 1).
- The mean age at the index date was 59 to 60 years in each country (Table 1).
- The median duration of observable follow-up was 18.2 months in the UK, 17.5 months in Germany, and 19.3 months in Spain.

Concurrent Chemoradiation

- The mean (SD) duration of the index chemoradiation treatment was 2.4 (1.5) months in the UK, 2.1 (1.0) months in Germany, and 2.1 (1.1) months in Spain. The median number of cycles administered was 3 in the UK and Spain and 2 in Germany (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, 90.7%, 83.9%, and 88.1% of patients in the UK, Germany, and Spain, respectively, had a performance status of 0 or 1 (Table 3).
- In all three countries, the most frequently administered chemotherapies was cisplatin with vinorelbine (UK, 40.1%; Germany, 29.7%; Spain, 39.6%) (Figure 2).
  - Most patients received the index chemoradiation in accordance with National Comprehensive Cancer Network (UK, 40.1%; Germany, 44.5%; Spain, 53.5%) and/or European Society for Medical Oncology (UK, 45.1%; Germany, 76.1%; Spain, 64.8%) guidelines.
- Across all countries, most patients stopped the index chemoradiation treatment due to completion of the planned course of treatment (UK, 92.0%; Germany, 81.9%; Spain, 83.5%) (Table 3).

Additional Treatment for Unresectable, Locally Advanced, Stage III NSCLC

- In the UK, Germany, and Spain, 42.0%, 30.3%, and 22.6% of patients received additional treatment for stage III disease after the index chemoradiation. Among these patients, 85.3% (UK), 95.7% (Germany), and 83.3% (Spain) received chemotherapy alone, and 2.9% (UK), 2.1% (Germany), and 11.1% (Spain) received additional chemoradiation. Patients who received chemotherapy (alone or with radiation) received a median of 3 to 3.5 cycles (Table 3).
- The most frequently received chemotherapies after the index chemoradiation were cisplatin with vinorelbine in the UK (15.0%), cisplatin with pemetrexed (21.7%) in Germany, and docetaxel in Spain (20.6%) (Figure 2).
- In the UK and Germany, most patients stopped the first treatment after the index chemoradiation due to completion of the planned treatment course (65.1% and 51,3%, respectively), while 20.6% and 35.9% stopped due to disease progression. In Spain, 46.9% stopped due to progressive disease and 34.4% stopped due to completion of the planned treatment (Table 3).

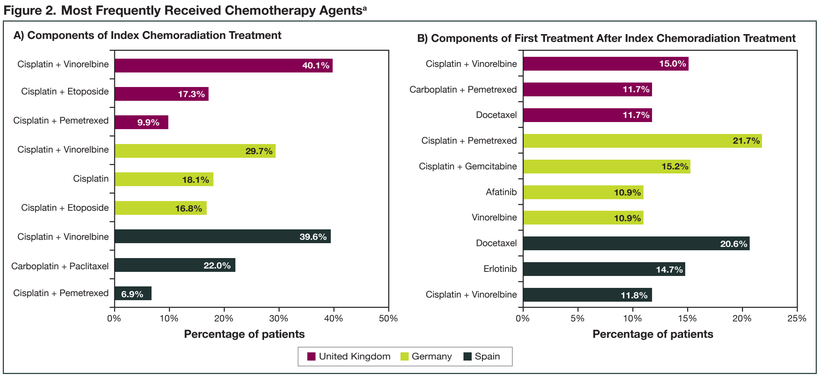
Treatment for Metastatic Disease

- During available follow-up, 42 (UK), 58 (Germany), and 35 (Spain) patients developed distant metastases.
- Of these patients, 61.9% (UK), 62.1% (Germany), and 45.7% (Spain) received chemotherapy and 21.4% (UK), 19.0% (Germany), and 31.6% (Spain) received biologics or other targeted therapies.
- During available follow-up, 86.1% (UK), 89.6% (Germany), and 70.4% (Spain) received only one line of systemic therapy; the remaining received two or more lines.

Health Care Resource Utilization

- During the index chemoradiation treatment, 74.1% (UK), 78.1% (Germany), and 67.6% (Spain) of patients had health care utilization information documented in their medical record. Among them, patients had a monthly median of 0.8 (UK), 1.4 (Germany), and 1.1 (Spain) NSCLC-related visits.
- During the first treatment after chemoradiation, 57.4% (UK), 59.6% (Germany), and 66.7% (Spain) of patients had documented health care utilization, with a median of 0.7 (UK), 1.3 (Germany), and 1.0 (Spain) NSCLC-related visits.

Figure 2. Most Frequently Received Chemotherapy Agents[a]



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

Table 3. Treatment Characteristics

Characteristic	UK				Germany				Spain			
	Index Chemoradiation		First Treatment After Chemoradiation		Index Chemoradiation		First Treatment After Chemoradiation		Index Chemoradiation		First Treatment After Chemoradiation	
Total patients initiating treatment (N, %)	162	100%	68	100%	155	100%	47	100%	159	100%	36	100%
Total patients discontinuing treatment (n, %)	162	100%	63	92.7%	155	100%	39	83.0%	158	99.4%	32	88.9%
Chemoradiation (n, %)	162	100%	2	2.9%	155	100%	1	2.1%	159	100%	4	11.1%
Duration in months (mean, SD)[a]	2.4	1.5	2.8	0.0	2.1	1.0	0.6		2.1	1.1	1.3	1.0
Chemotherapy only (n, %)	0	0%	58	85.3%	0	0%	45	95.7%	0	0%	30	83.3%
Duration in months (mean, SD)[a]			2.6	2.2			2.7	1.9			3.5	2.5
Radiotherapy only (n, %)	0	0%	8	11.8%	0	0%	1	2.2%	0	0%	2	5.6%
Duration in months (mean, SD)[a]			1.4	1.2			0.5				0.4	0.1
Performance status of 0 or 1 at start of treatment	147	90.7%	55	80.9%	130	83.9%	31	66.0%	140	88.1%	20	55.6%
Number of cycles (median)	3.0		1.0		2.0		3.0		3.0		3.5	
Reason for stopping treatment[a,b]												
Adverse event	1	0.6%	2	3.2%	0	0%	1	2.6%	2	1.3%	0	0%
Patient decision	2	1.2%	4	6.4%	5	3.2%	4	10.3%	7	4.4%	3	9.4%
Progressive disease	8	4.9%	13	20.6%	23	14.8%	14	35.9%	12	7.6%	15	46.9%
Completion of planned course of treatment	149	92.0%	41	65.1%	127	81.9%	20	51.3%	132	83.5%	11	34.4%
Loss to follow-up	0	0%	1	1.6%	0	0%	0	0%	2	1.2%	0	0%
Death	0	0%	0	0%	0	0%	1	2.6%	2	1.3%	3	9.4%
Other	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Don't know	3	1.9%	3	4.8%	0	0%	1	2.6%	3	1.9%	1	3.1%

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

Table 2. Sample Characteristics

Characteristic	UK		Germany		Spain	
Number of patients (N, %)	162	100%	155	100%	159	100%
Male (n, %)	105	64.8%	102	65.8%	125	78.6%
White (n, %)	145	89.5%	149	96.1%	157	98.7%
Age at index date, years (mean, SD)	59.6	8.8	59.1	7.8	59.0	8.3
Median	59.8		59.3		59.3	
Stage at initial diagnosis (n, %)						
Stage IIB	1	0.6%	0	0.0%	2	1.3%
Stage IIIA	95	58.6%	83	53.6%	56	35.2%
Stage IIIB	66	40.7%	72	46.5%	101	63.5%
Tumor histology (n, %)[a]						
Adenocarcinoma	83	51.2%	74	47.7%	76	47.8%
Large cell carcinoma	3	1.9%	1	0.7%	16	10.1%
Squamous cell carcinoma	73	45.1%	79	51.0%	64	40.3%
Unknown	2	1.2%	1	0.7%	0	0.0%
Tumor grade at initial diagnosis (n, %)[a]						
Grade 1	4	2.5%	14	9.0%	13	8.2%
Grade 2	56	34.6%	73	47.1%	93	58.5%
Grade 3	59	36.4%	33	21.3%	31	19.5%
Grade 4	5	3.1%	6	3.9%	8	5.0%
Could not be assessed/unknown	38	23.5%	29	18.7%	14	8.8%
PD-L1 testing at initial diagnosis (n, %)						
Yes	19	11.7%	15	9.7%	8	5.0%
Met test threshold for PD-L1 expression among tested	6	31.6%	12	80.0%	4	50.0%
No	134	82.7%	138	89.0%	150	94.3%
Unknown	9	5.7%	2	1.3%	1	0.6%
Performance status of 0 or 1 at index date (n, %)	146	90.1%	128	82.6%	142	89.3%
Charlson Comorbidity Index score (mean, SD)[b]	1.0	1.1	1.0	1.0	0.8	0.9
Smoking status						
Current smoker	34	21.0%	43	27.7%	43	27.0%
Former smoker	100	61.7%	93	60.0%	89	56.0%
Nonsmoker	22	13.6%	13	8.4%	24	15.1%
Unknown	6	3.7%	6	3.9%	3	1.9%

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

CONCLUSIONS

- In this study, patients treated with concurrent chemoradiation generally initiated treatment according to guidelines.
- In the UK and Germany, most patients completed definitive chemoradiation therapy as planned. A substantial proportion of patients receive additional treatment after the index chemoradiation treatment and stopped due to disease progression, particularly in Spain.
- 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. Eberhardt WE, De Ruysscher D, Weder W, et al. 2nd ESMO consensus conference in lung cancer: locally advanced stage III non-small-cell-lung cancer. Ann Oncol. 2015 Aug;26(8):1573-88.
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.

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