Treatment patterns and survival in patients with small cell lung cancer in Taiwan

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Abstract

Background: Small cell lung cancer (SCLC) is the most aggressive form of lung cancer. The chemotherapy regimens and their efficacy in practice are seldom reported. We aimed to investigate treatment patterns and survival outcomes of patients with SCLC in Taiwan.

Methods: Patients newly diagnosed with SCLC from 2011 to 2015 were identified from the Cancer Registry database. Their clinical characteristics, treatment regimens, and survival status were obtained from National Health Insurance Research database. The Kaplan–Meier method and Cox-proportional hazard model were used to analyze the survival outcomes.

Results: Among a total of 2707 patients enrolled, 439 were in the limited stage (LS, 16.22%) and 2268 were in the extensive stage of the disease (ES, 83.78%). The median age was 66 and the majority were male (90.36%). The first-line regimen used for the patients was etoposide/cisplatin-based treatment, followed by etoposide/carboplatin-based regimen, and etoposide only. The median overall survival (OS) was 16.92 months (95% confidence interval [CI] 15.31–18.92) and 8.71 months (95% CI 8.38–9.07) in LS and ES patients, respectively. Chemotherapy regimen, Eastern Cooperative Oncology Group performance status, and history of radiotherapy were significant factors associated with OS. On the other hand, the major second-line treatment was a topotecan-based regimen (68.3%). However, this showed inferior survival outcome compared to etoposide-based regimen (5.09 months [95% CI 4.76–5.62] versus 8.77 months [95% CI 6.31–11.89], $p < 0.001$).

Conclusion: Etoposide is the preferred and superior first-line chemotherapy regimen in combination with platinum, and an alternative choice of second-line regimen for Taiwanese patients with SCLC.

Keywords: Chemotherapy; Small cell lung cancer; Topotecan

1. INTRODUCTION

Small-cell lung cancer (SCLC) comprises about 15% of all lung cancers and is characterized by rapid growth and early metastasis. According to the Veterans Affairs Lung Study Group staging system, SCLC patients are classified as limited-stage (LS) or extensive-stage (ES) patients. Approximately two-thirds of SCLC patients in the United States and Taiwan are classified as ES patients upon diagnosis.[1,2]

Platinum-based doublet chemotherapy consisting of cisplatin or carboplatin plus etoposide has been the standard treatment for ES-SCLC patients for more than 30 years, with a response rate of up to 70%. On the other hand, concurrent chemoradiotherapy with cisplatin and etoposide is the preferred management of LS-SCLC, with a response rate around 70%–90%.[3] Despite initial sensitivity to chemotherapy and radiotherapy, most patients eventually experience recurrence of the cancer within a few months.[1,3] The median OS time of ES-SCLC is less than 1 year, with a 2-year survival rate of less than 5%, and 5-year survival rate of less than 2%.[4]

Topotecan, a topoisomerase I inhibitor, is the preferred chemotherapy regimen for relapsed SCLC.[5,6] However, the response rate of single-agent topotecan for relapsed SCLC remains at only 5% given a treatment-free interval within 3 months.[7] On the other hand, an original chemotherapy regimen can be used if the treatment-free interval is more than 6 months.[8] Only a subset of patients can proceed to the second-line (2L) treatment due to the aggressive disease course and some patients opting to receive palliative care only. Consequently, treatment patterns and survival outcomes for patients with relapsed SCLC were seldom reported.

In Taiwan, SCLC is the most aggressive form of lung cancer. Previous research showed that the median survival time for Taiwanese patients with LS and ES SCLC were 10.3 and 5.6 months upon diagnosis, respectively.[2] However, this was only based from data gathered between years 2004 and 2006. Furthermore, previous data regarding chemotherapy regimens were not available. In this study, by linking the National Health

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Insurance Research database and the Cancer Registry database, we aim to describe the demographics, clinical characteristics, and treatment outcomes of patients with LS-SCLC and ES-SCLC in Taiwan.

2. METHODS

2.1. Data source

The data was gathered from three databases provided by the Health & Welfare Data Science Center (HWDSC): Taiwan Cancer Registry (TCR) Database 2002–2015, National Health Insurance Research Database (NHIRD) 2010–2017, and Death registry 2002–2017.

Established in 1979, the TCR is organized and funded by the Ministry of Health and Welfare, and it is managed by Taiwan Public Health Association. All hospitals in Taiwan with at least 50 beds are mandated to report all newly diagnosed and confirmed malignancies to the registry. Detailed information (so-called long-form reporting) on provision of care, treatments, and outcomes is collected from a total of 80 hospitals, covering more than 90% of all cancer cases diagnosed annually in Taiwan. Diagnoses are coded according to the International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) format.

NHIRD was established since National Health Insurance (NHI), a mandatory social insurance program covering virtually all the population in Taiwan, was launched in 1995. It includes claim data submitted by healthcare organizations, and information about the characteristics of healthcare providers (healthcare organizations and professionals) as well as insured individuals.

We used the NHIRD claim data to identify key variables, including primary and secondary diagnoses (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] format), and specific treatments for SCLC including chemotherapy prescribed during outpatient visits or hospital admissions. If the patient has died, the date of death was identified in the Death Registry.

2.2. Study subjects

Patients newly diagnosed with lung cancer (ICD-O-3 codes C33.9 and C34.X; Histological code in 8041, 8042, 8043, and 8044) from January 1, 2011, to December 31, 2015, were identified from the TCR database. Criteria for exclusions were unknown diagnosis date, less than 20 years of age, TNM stage 0 or unknown, unidentifiable classification (limited or extensive), diagnosed with other types of cancer or other cell types of lung cancer in the past 5 years, no treatment received after diagnosis, and diagnosis not confirmed by pathology.

The TCR data of the selected patients were then linked to the data in NHIRD to define their treatment cohorts. Data were excluded if the patient did not have any prescription of chemotherapy in the claimed database, did not receive chemotherapy within 6 months after diagnosis, received one session of chemotherapy only, the received second-line chemotherapy drug at the first-line treatment, had indistinguishable treatment switches, or received only cisplatin or target therapy as the first-line treatment.

2.3. Determination of stage

TCR used the American Joint Committee on Cancer staging system, 7th edition to record the stages of all cancer patients. However, the Veteran's Administration Lung Group 2-Stage System was used to define the tumor extent in patients with SCLC. Due to this, we converted the TNM stages of these patients to LS or ES depending on set criteria. If N = 0–2 or M = 0, then it was defined as LS. On the other hand, if N = 3 or M = 1, then it was defined as ES.[2] The final number of patients available for analysis was 439 for limited stage, and 2268 for extensive stage. The patient selection process was listed in Supplementary Figure 1, http://links.lww.com/JCMA/A84.

2.4. Treatment regimens and treatment lines

We defined the index date of first-line (1L) treatment as the date of the first documented prescription of chemotherapy drugs after diagnosis. To classify the types of prescribed 1L treatment regimens, we analyzed the patients' chemotherapy status within 42 days after the index date. Etoposide was categorized as the primary chemotherapy drug, cisplatin and carboplatin were categorized as the secondary, and the rest were grouped as others. Cumulatively, the 1L regimens can be classified into cisplatin-based regimen, involving etoposide (intravenous or oral) plus cisplatin; carboplatin-based regimen, involving etoposide (intravenous or oral) plus carboplatin; etoposide only (intravenous or oral), and others (including cyclophosphamide, fluorouracil, gemcitabine, vincristine, and vinorelbine). The detailed list of prescribed regimens may be found in Supplementary Table 1, http://links.lww.com/JCMA/A84.

We defined the start (index date) of the second-line (2L) treatment regimen as either an augmenting or switching of chemotherapy following the 1L treatment or the initiation of the same 1L regimen after it had been discontinued for more than 180 days. If within 180 days, it would be treated as the continuation of 1L treatment.

Among the 2L regimens, topotecan and etoposide were categorized as primary chemotherapy drugs, and the rest were classified under others. The 2L regimens were classified into topotecan-based regimen (topotecan only; topotecan plus cisplatin or carboplatin; topotecan plus others), etoposide-based regimen (etoposide only; etoposide plus cisplatin/carboplatin; etoposide plus others), and others (including cyclophosphamide, tegafur, vinorelbine, docetaxel, methotrexate, paclitaxel, pemetrexed, doxorubicin, mitomycin, paclitaxel, cytarabine, dacarbazine, and melphalan). The detailed list of 2L regimen may be found in Supplementary Table 2, http://links.lww.com/JCMA/A84.

2.5. Outcome measurements and other control variables

For the OS analysis, patients were censored at death or at the end of follow-up, December 31, 2017, whichever came first. OS was calculated from the date of diagnosis to the date of death due to any cause or the end of follow-up.

Other control variables included patients' characteristics (age, sex, year of diagnosis, and physical performance before treatment), acquisition of radiation therapy (recorded in TCR database), and hospital accreditation levels. We used the Eastern Cooperative Oncology Group (ECOG) Performance Status scores to measure patients' physical performance. An ECOG score of 0 means fully active, 1 means restricted in physically strenuous activity, 2 means ambulatory and capable of all self-care, 3 means capable of only limited self-care, and 4 means completely disabled. We classified patients' ECOG Performance status into three groups: 0–1, ≥2, and unknown. The Institutional Review Board of Taipei Medical University approved this study (IRB No. 201911015)

2.6. Statistical analysis

We used frequencies and percentages for categorical variables and the mean ± standard deviation for variables measured in continuous or interval scales. The Kaplan–Meier method and the log-rank test were used to examine the survival outcome between treatment regimens. Cox-proportional hazard model was used to determine the adjusted HRs of death. The p value

<0.05 was considered statistically significant. All analyses were performed using SAS for Windows, version 9.4 (SAS Institute, Inc., Cary, NC).

3. RESULTS

3.1. Patient characteristics

Patient characteristics are listed in Table 1. The median age of all 2707 SCLC patients was 66 years old and the majority were male (90.36%). Most of the patients had ECOG PS 0-1 (68.56%). Few patients received operations after diagnosis (5.39%), and the percentage is higher in patients with limited stage (10.02%). Around half of the patients had history of radiotherapy (51.16%), and the percentage was higher for those in limited stage (62.64%). Most patients received treatment at district hospitals (52.49%). In patients with LS-SCLC, no significant difference was found in the distributions of age, ECOG PS and treatment regimen between different hospital levels (Supplementary Table 3, http://links.lww.com/JCMA/A84).

3.2. First-line systemic treatments and outcomes

The distribution of 1L treatment regimen for patients in LS and ES are shown in Supplementary Figures 2a and b, http://links.lww.com/JCMA/A84. The major regimen used in LS and ES patients was cisplatin-based treatment (78.59% and 81.08%), followed by carboplatin-based treatment regimen (12.07% and 10.36%), and etoposide only treatment regimen (8.66% and 7.54%). The patients who received cisplatin-based regimen tended to be younger and had better performance status compared to those who received etoposide only (Supplementary Table 4, http://links.lww.com/JCMA/A84).

Table 1

Baseline characteristics of small cell lung cancer patients

	Total		Limited stage		Extensive stage	
	N	%	N	%	N	%
Total	2707	100.00	439	16.22	2268	83.78
Age						
Median (Q1, Q3)	66 (60, 75)		67 (60, 75)		66 (59, 75)	
Gender						
Male	2446	90.36	399	90.89	2047	90.26
Female	261	9.64	40	9.11	221	9.74
Year at diagnosis						
2011	561	20.72	91	20.73	470	20.72
2012	533	19.69	84	19.13	449	19.80
2013	539	19.91	81	18.45	458	20.19
2014	510	18.84	90	20.50	420	18.52
2015	564	20.83	93	21.18	471	20.77
Operation						
Yes	146	5.39	44	10.02	102	4.50
No	2561	94.61	395	89.98	2166	95.50
Radiation therapy						
Yes	1385	51.16	275	62.64	1110	48.94
No	1322	48.84	164	37.36	1158	51.06
ECOG PS						
0-1	1856	68.56	354	80.64	1502	66.23
≧2	600	22.16	47	10.71	553	24.38
Unknown	251	9.27	38	8.66	213	9.39
Accreditation level of hospital						
Medical Center	863	31.88	152	34.62	711	31.35
Regional Hospital	423	15.63	75	17.08	348	15.34
District Hospital	1421	52.49	212	48.29	1209	53.31

For patients with LS, the median OS was 16.92 months (95% confidence interval [CI] 15.31–18.92). The 1- and 2-year survival rates were 62.3% and 33.5%, respectively. The median OS for patients receiving cisplatin-based or carboplatin-based regimen were respectively, 16.79 months (95% CI 14.88–19.35) and 15.57 months (95% CI 9.63–21.55). These were better than 9.33 months (95% CI 5.62–10.32) among patients receiving etoposide only ($p < 0.0001$ and 0.006, respectively, Fig. 1A). In the adjusted Cox regression model (Table 2), when other variables were controlled, the cisplatin-based regimen had a lower hazard ratio (HR) (0.66) compared to the reference regimen (Etoposide only). The carboplatin-based regimen also showed lower HR (0.65), but the p value (0.065) is not statistically significant. Among the control variables, patients had higher HR if they were over 80 years old, with ECOG PS level 2 or above and treated in regional or district hospitals. Patients receiving radiotherapy had lower HR.

For patients with ES, the median OS was at 8.71 months (95% CI 8.38–9.07). The 1- and 2-year survival rates were 33.3% and 10.8%, respectively. The median OS of patients receiving cisplatin-based regimen was 8.44 months (95% CI 8.08–8.80), which was longer than 7.23 months (95% CI 6.18–8.02) in patients receiving carboplatin-based regimen, 4.17 months (95% CI 3.32–4.76) in patients using etoposide-only regimen, and 5.16 months (95% CI 2.66–7.62) in patients using other regimens (Fig. 1B). In the adjusted Cox regression model (Table 3), Cisplatin-based and carboplatin-based regimens had lower HR (0.81 and 0.75) when compared to the reference regimen (Etoposide only). Patients had higher HRs if they were male, over 70 years old, with higher ECOG PS level, without radiotherapy, and treated in regional or district hospitals.

3.3. Second-line systemic treatments and outcomes

The major 2L regimen was topotecan-based treatment (68.30%). Etoposide-based treatment had 12.52%, and others 19.18% (Supplementary Figure 3, http://links.lww.com/JCMA/A84). Eighty LS patients and 183 ES patients started to receive 2L regimens 180 days or more after 1L treatment, 43 (53.75%) and 89 (48.63%) of them received the etoposide-based regimen. The median OS of patients receiving etoposide-based regimen as 2L therapy was at 8.77 months (95% CI 6.31–11.89), which was better than 5.09 months (95% CI 4.76–5.62) in patients receiving topotecan-based regimen, and 4.63 months (95% CI 4.01–5.52) in patients using other regimen (Fig. 2). In the adjusted Cox regression model including the timing of treatment switch as a parameter (Table 4), the HR is similar between treatment regimens. Patients showed lower HR if the timing of treatment switch is more than 180 days. Patients showed higher HR if they were over 80 years old, with higher ECOG PS level, in ES upon diagnosis, and treated in regional or district hospitals.

4. DISCUSSION

We demonstrated the actual treatment patterns of SCLC in Taiwan. Etoposide plus platinum was the preferred 1L chemotherapy regimen in both LS- and ES-SCLC, and it had superior efficacy compared to etoposide alone. Topotecan is the preferred 2L regimen in relapsed SCLC. However, it showed limited efficacy and had inferior survival outcome compared to the etoposide-based regimen.

More than 80% of the patients in our cohort were ES at diagnosis. This proportion was higher than the previous literature, of which 70% of SCLC patients were ES.[1,9] This may have been affected by the difference in the definition of stages. The patients' stages in our cohort were converted from TNM stages, and patients with N3 disease were classified to ES. Using the

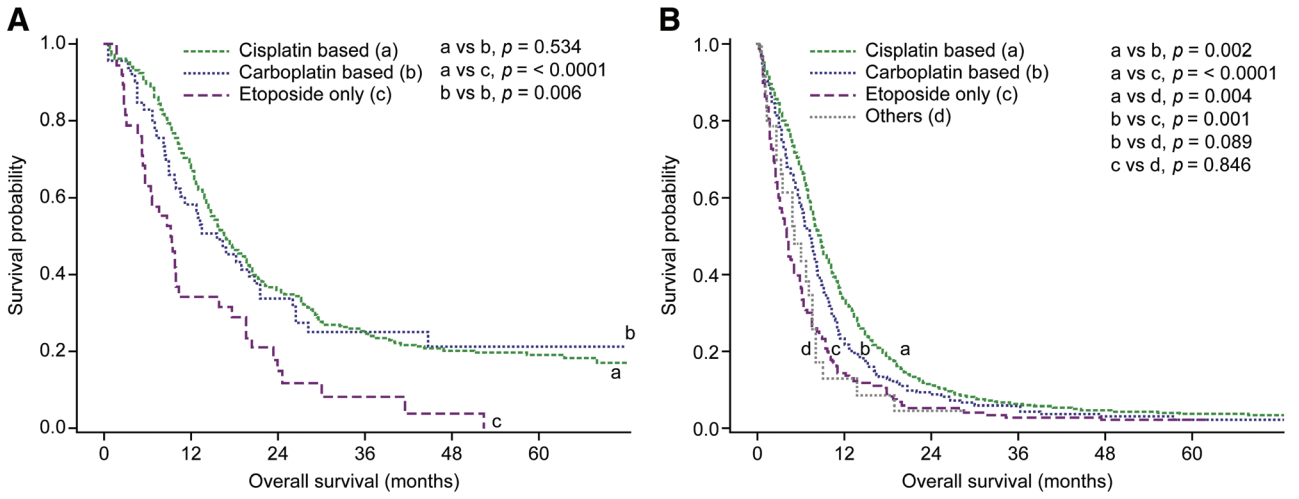

Fig. 1 Survival outcome. Overall survival (OS) by first-line treatment for small cell lung cancer (SCLC) patients (A) limited stage and (B) extensive stage.

same classification, the percentage of ES was higher than previous research done in Taiwan.[2] This may be due to the advancements in diagnostic modalities, such as magnetic resonance imaging and positron emission tomography (PET). Previous studies had shown that the utility of PET upstaged around 10% of patients with LS-SCLC to ES.[10,11] Since most patients with SCLC in Taiwan are classified under ES at diagnosis, improving the efficacy of systemic treatment is important for dealing with this lethal disease.

The median OS time of LS- and ES-SCLC patients in our cohort was 16.92 and 8.71 months, respectively. These results were similar to the those of a recent systemic review and better than our previous report.[2,12] This may have been caused by the exclusion criteria, allowing only patients who received systematic treatment. In a previous report, some lung cancer patients chose not to receive cancer treatment despite having NHI coverage, and consequently a worse prognosis was expected.[13] Etoposide plus cisplatin was the preferred 1L chemotherapy regimen in both LS- and ES-SCLC patients and was associated with better survival compared to etoposide alone. Our findings confirmed the role of etoposide plus platinum as the standard-of-care in 1L chemotherapy for SCLC. Previous meta-analysis showed

Table 2

Adjusted cox proportion regression model analysis for first-line treatment of limited-stage small cell lung cancer patients

	N	Hazard ratio	95% Confidence interval		p
Treatment regimens					
Etoposide-only	38	1 (Ref)			
Cisplatin-based	345	0.66	0.45	0.98	0.039
Carboplatin-based	53	0.65	0.41	1.03	0.065
Others	3	1.21	0.36	4.07	0.754
Gender					
Male	399	1 (Ref)			
Female	40	0.69	0.46	1.01	0.058
Age, y					
20–49	24	1 (Ref)			
50–59	86	0.89	0.53	1.52	0.677
60–69	145	0.98	0.59	1.63	0.943
70–79	133	1.23	0.74	2.05	0.422
≧80	51	1.86	1.03	3.34	0.039
ECOG PS level					
0–1	354	1 (Ref)			
≧2	47	1.74	1.24	2.44	0.001
Unknown	38	1.17	0.80	1.71	0.428
Accreditation level of hospital					
Medical center	152	1 (Ref)			
Regional hospital	75	1.56	1.13	2.15	0.007
District hospital	212	1.33	1.04	1.71	0.024
Radiation therapy during 1L treatment					
No	275	1 (Ref)			
Yes	164	0.77	0.61	0.97	0.024

Table 3

Adjusted cox proportion regression model analysis for first-line treatment of extensive-stage small cell lung cancer patients

	N	Hazard ratio	95% Confidence interval		p
Treatment regimens					
Etoposide-only	171	1 (Ref)			
Cisplatin-based	1839	0.81	0.69	0.96	0.017
Carboplatin-based	235	0.75	0.62	0.92	0.006
Others	23	1.18	0.76	1.85	0.465
Gender					
Male	2047	1 (Ref)			
Female	221	0.81	0.70	0.93	0.004
Age, y					
20–49	129	1 (Ref)			
50–59	436	0.96	0.78	1.18	0.673
60–69	729	1.19	0.97	1.45	0.091
70–79	681	1.51	1.23	1.85	<0.0001
≧80	293	1.83	1.46	2.31	<0.0001
ECOG PS level					
0–1	1502	1 (Ref)			
≧2	553	1.60	1.45	1.78	<0.0001
Unknown	213	1.33	1.15	1.55	0.0002
Accreditation level of hospital					
Medical center	711	1 (Ref)			
Regional hospital	348	1.15	1.01	1.31	0.042
District hospital	1209	1.10	1.00	1.21	0.053
Radiation therapy during 1L treatment					
No	1158	1 (Ref)			
Yes	1110	0.69	0.63	0.75	<.0001

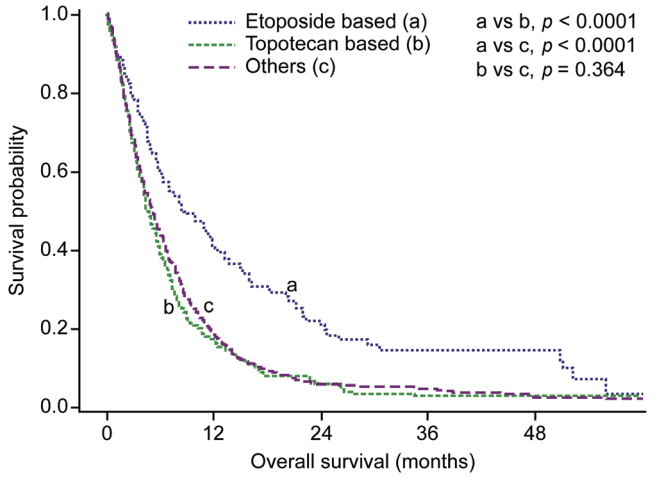

Fig. 2 Overall survival (OS) by second-line treatment for small cell lung cancer (SCLC) patients.

Table 4

Adjusted cox proportion regression model analysis for second-line treatment of small cell lung cancer patients

Parameter	N	Hazard ratio	95% Confidence interval		p
Treatment regimens					
Topotecan-based	851	1 (Ref)			
Etoposide-based	156	0.86	0.68	1.09	0.200
Others	239	1.04	0.90	1.21	0.595
Gender					
Male	1120	1 (Ref)			
Female	126	0.82	0.67	1.00	0.049
Age, y					
20–49	101	1 (Ref)			
50–59	323	0.94	0.74	1.19	0.624
60–69	426	1.05	0.83	1.32	0.700
70–79	311	1.17	0.93	1.49	0.184
≧80	85	1.58	1.17	2.13	0.003
ECOG PS level					
0–1	984	1 (Ref)			
2	172	1.29	1.09	1.52	0.004
Unknown	90	1.10	0.88	1.38	0.406
Stage in initial diagnosis					
Limited stage	1028	1 (Ref)			
Extensive stage	218	1.44	1.23	1.69	<0.0001
Accreditation level of hospital					
Medical center	527	1 (Ref)			
Regional hospital	233	1.31	1.11	1.54	0.002
District hospital	486	1.36	1.19	1.55	<0.0001
Timing of treatment switch					
Within 180 d	975	1 (Ref)			
More than 180 d	271	0.58	0.48	0.70	<0.0001

that there is no difference in the efficacy between cisplatin and carboplatin in the first-line treatment of SCLC.[14] However, for ES-SCLC patients in our database, a cisplatin plus etoposide regimen showed better OS compared to carboplatin plus etoposide in Kaplan–Meier analysis. This finding may be partly related to the regulation of Taiwan's national health insurance. Carboplatin can only be used in patients with impaired renal function (creatinine clearance rate less than 60 ml/h). Patients who received cisplatin plus etoposide could have had more favorable prognostic factors at baseline. Recently, two phase 3 randomized trials showed that programmed death ligand (PDL1) inhibitors, such as atezolizumab or durvalumab, in combination with etoposide plus platinum chemotherapy as 1L treatment significantly improved OS in ES-SCLC.[15,16] Whether cisplatin plus etoposide is the preferred chemotherapy regimen in Taiwanese patients with SCLC in the era of immunotherapy needs further investigation.

Topotecan is the only FDA approved subsequent chemotherapy in relapsed SCLC. A previous meta-analysis showed that the 1-year survival rate after topotecan is around 9%–27%.[7] In our study, topotecan-based chemotherapy was the preferred regimen in the second-line setting and the 1-year survival rate was 18.5%, which was comparable with previous reports. However, it showed an inferior survival outcome compared to etoposide in our cohort. It can be explained partly by the difference of tumor nature, patients who received topotecan may have more aggressive disease course compared to the patients who received etoposide regimen. In the adjusted Cox regression model including the timing of treatment switch as a parameter, the HR is similar between treatment regimens. Previous retrospective studies also revealed that patients who re-used platinum doublet chemotherapy had longer survival rates as compared to monotherapy.[17,18] In our cohort, the etoposide-based regimen was used mostly after 180 days after the first regimen. NCCN guidelines suggested that patients, whose relapses happened more than 6 months after the first-line treatment was administered, are considered platinum-sensitive and are recommended to be re-challenged with etoposide-platinum combination therapy.[6] However, a significant portion of our patients received topotecan even after 180 days following the first-line therapy. Our finding was consistent with a previous multicountry study. By using a global database, DiBonaventura et al[19] found that approximately half of patients were not re-challenged with a platinum-based therapy in platinum-sensitive patients. Recently, a phase 3 trial also demonstrated that carboplatin plus etoposide rechallenge had better response rate and progression-free survival compared to topotecan in patients with sensitive relapsed SCLC.[20] Limited treatment opinions and lack of consensuses were the main obstacles in the 2L treatment of SCLC. New drugs and new combinations are urgently needed to improve outcomes for SCLC patients after failure of 1L treatment. Novel cytotoxic drugs, such as lurbinectedin or immune-checkpoint inhibitors, may shed some light in this area.[21,22]

The combination of radiotherapy and platinum-based chemotherapy is the standard of care for LS-SCLC.[1] The impact of radiotherapy in survival outcome for patients with ES-SCLC remains questionable. Previous trial showed that consolidation thoracic radiotherapy led to better intrathoracic control and better 2-year OS in ES-SCLC.[23] In our study, 62.64% of LS patients and 48.94% of ES received radiotherapy during 1L systemic treatment. After cox proportion regression analysis, radiotherapy provided better survival outcome in both LS and ES SCLC patients. However, the database we used did not have detailed information about radiotherapy. Further studies are needed to elucidate the role of radiotherapy, especially in ES-SCLC patients.

Besides chemotherapy regimen and history of radiotherapy, our study also found other prognostic factors in survival analysis. Old age and poor performance status were well-known poor prognostic factors in SCLC[24] and were also demonstrated in our study. In addition to clinical factors, we also included the accreditation level of hospitals in the analysis. More than 50% of our patients received treatment in district hospitals, reflecting patient's healthcare seeking behavior and the distributions of hospitals in Taiwan. In our study, patients who received treatment in medical centers tended to have better survival compared

to those treated in regional or district hospitals. Further research is needed to validate this finding. Nevertheless, similar findings were found in the literature discussing other cancer types, both in Taiwan and worldwide.[25–27] Patients who were treated in medical centers may have had more chance to receive multimodality treatments and participate in clinical trials. Allocation of the treatment resources may be an issue to improve survival outcome in Taiwanese SCLC patients.

This study had several limitations. First, important information about 1L treatment such as the responses, reasons of termination, and the exact progression-free survival time were lacking. Some laboratory prognostic factors, such as lactate dehydrogenase level, were also unavailable. We found that radiotherapy was a key factor for prolonged survival, but the detailed information on radiotherapy is not available in our database. The actual impact of different radiotherapy (eg, thoracic radiation or cranial irradiation) on OS in our cohort is hard to evaluate. Nevertheless, our study presents the largest observational population-base cohort related to the treatment pattern and survival of SCLC patients in Taiwan.

In conclusion, our study showed that etoposide is a preferred and superior 1L chemotherapy regimen in combination with platinum among Taiwanese SCLC patients. Furthermore, it was also shown to be an alternative 2L regimen in some patients.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://doi.org/10.1097/JCMA.0000000000000264.

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