Real-World Treatment Patterns, Healthcare Resource Utilization and Clinical Outcomes of Patients with Extensive-Stage Small-Cell Lung Cancer in Alberta, Canada

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BACKGROUND and Objectives

- Small cell lung cancer (SCLC) is an aggressive lung cancer subtype with neuroendocrine differentiation that accounts for 10% to 15% of lung cancers [1,2].
- Approximately 70% of patients are diagnosed with extensive stage (ES) disease [1].
- In Canada, the recommended first-line systemic therapy for patients with ES SCLC is platinum (cisplatin or carboplatin) + etoposide in combination with one of the programmed death-ligand 1 (PD-L1) inhibitors, durvalumab or atezolizumab that started being publicly reimbursed as frontline treatment for patients with ES SCLC in 2022.
- Second-line treatments include rechallenge with platinum + etoposide (in platinum-sensitive patients, based on chemotherapy-free interval [CFI]), cyclophosphamide + doxorubicin + vincristine (CAV), topotecan, or lurbinectedin[3,4].
- Median overall survival in 1L trials of PD-L1 inhibitor combinations is ~12 to 13 months which reduces significantly in subsequent lines of treatment thus, patients with ES-SCLC in relapsed setting have an urgent unmet medical need. Even with newer treatments, survival after second- or third-line treatment remains <1 year [5,6,7].

OBJECTIVES

- The objectives of this study were to describe the baseline characteristics, treatment patterns, and outcomes among individuals with de novo or recurrent ES-SCLC diagnosed in Alberta, Canada.

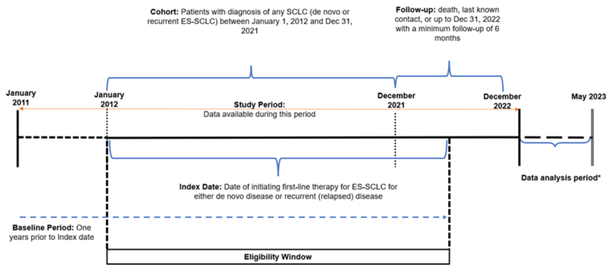
METHODS

- A retrospective, observational, cohort study leveraging the administrative databases and the cancer registry that provides coverage for the entire population of Alberta, Canada. was employed (Figure 1).
- Included in this database are a total of 17 cancer centers (2 tertiary, 4 regional, and 11 community hospitals) for the entire province of Alberta, under a public payer system.

Inclusion criteria

- Adult patients with a diagnosis of TNM stage IV SCLC or treatment for recurrent SCLC between January 2012 and December 2021 who initiated first-line therapy for ES-SCLC prior to 30 June 2022.

Figure 1: Study Design



Abbreviations: ES- SCLC; extensive stage small cell lung cancer, tx; treatment

Baseline Period: For every patient, the baseline period is 1-year prior to index date. *The period between January 01, 2011 to December 31, 2021 will be used to collect baseline data. In the schema, an example of the baseline period for a patient with an index date of January 01, 2012 is shown.* **Study Period**: Data from as early as January 01, 2011 through to December 31, 2022.

Table 1: Study endpoints

Endpoint	Description
Patient characteristics	Age, sex, socioeconomic status, Charlson co-morbidities
Treatment patterns	Time from diagnosis to 1L, 2L, and 3L treatment initiation, average number of lines of therapy, frequency of systemic therapy regimens, by line of treatment (LOT), treatment sequencing and attrition, time-to-treatment discontinuation (TTD) by LOT
Healthcare resource use	Hospitalizations, emergency and non-emergency ambulatory visits, non-cancer practitioner visits
Clinical outcomes	Real-world overall survival (rwOS), Time-to-treatment discontinuation (TTD) by LOT, time-to next treatment or death (TTNT/D) , by LOT

Abbreviations: LOT; line of therapy, PFS; progression-free survival, TTD; time-to-treatment discontinuation, TTNT/D; time-to-next treatment or death

Statistical analyses

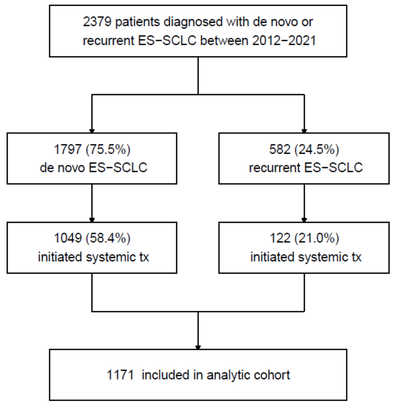
- All analyses were descriptive.
- Healthcare resource use was collected for up to 24 months in each line of treatment. Frequency of ER visits, ambulatory visits, and hospitalizations were reported in terms of mean, median, and standard deviation.
- Clinical outcomes were based on time-to-event data, so the Kaplan-Meier method was used for the analysis.

RESULTS

Study population

- 2379 patients with de novo or recurrent ES-SCLC were identified [Figure 2].
- Of these, 1171 (49.2%) initiated systemic therapy and were included in the analytical cohort.
- Most patients (58.4%) diagnosed with de novo ES-SCLC initiated treatment while only a minority of those (21.0%) with recurrent ES-SCLC initiated treatment.

Figure 2: Patient flow diagram



Abbreviations: ES- SCLC; extensive stage small cell lung cancer, tx; treatment . All individuals within the initial cohort who initiated systemic therapy did so prior to June 30, 2022

Baseline characteristics

- The mean age of patients at index date was 67.3 and there was an even split between males and females (51% vs. 49%).
- The majority (61.9%) of patients had more than 1 metastatic site at index with hepatic metastases being the most prevalent.

Table 2: Baseline characteristics

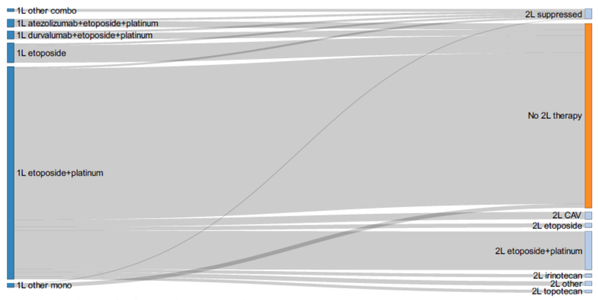
	Overall cohort (n= 1,171)
Age at index date, years (mean (SD))	67.3 (8.6)
Female (%)	574 (49.0)
Rural residence (%)	260 (22.2)
Nbh household income, $1K (mean (SD))	46.1 (19.1)
Nbh % highschool diploma (mean (SD))	78.0 (12.0)
1+ Charlson comorbidities (%)	807 (68.9)
2+ metastatic sites (%)	568 (61.9)
Hepatic metastasis (%)	408 (44.5)
Pleura metastasis (%)	345 (37.6)
Bone metastasis (%)	316 (34.5)
Lymph node metastasis (%)	191 (20.8)
Adrenal metastasis (%)	183 (20.0)
Brain metastasis (%)	181 (19.7)
Pulmonary metastasis (%)	144 (15.7)
Other metastasis (%)	142 (15.5)
Peritoneum metastasis (%)	47 (5.1)
Surgery prior to 1L (%)	14 (1.2)
Radiation prior to 1L (%)	186 (17.8)

Abbreviations:1L; 1st line, SD; standard deviation
Estimates for neighborhood household income are reported in units 1,000 dollars CAD (e.g., an estimate of 50 would correspond to 50,000 dollars CAD)

Treatment patterns

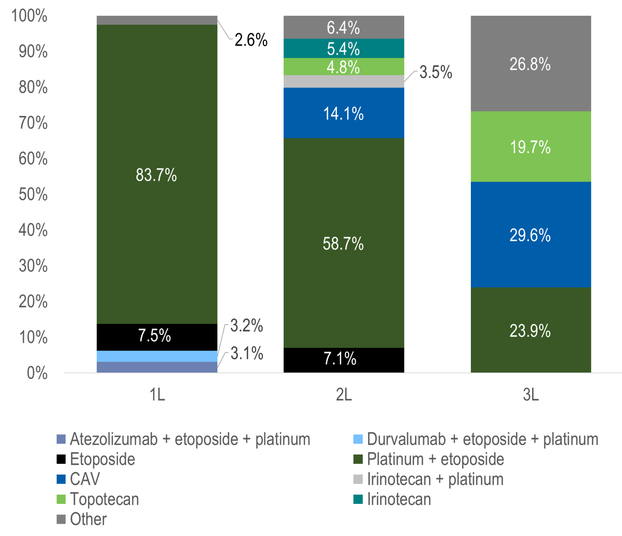
- Attrition between lines of treatment was high; of the 1171 initiating 1st line (1L) treatment, only 312 (26.6%) and 71 (6.1%) received 2nd line (2L) and 3rd line (3L) treatment , respectively.

Figure 3:Sankey diagram



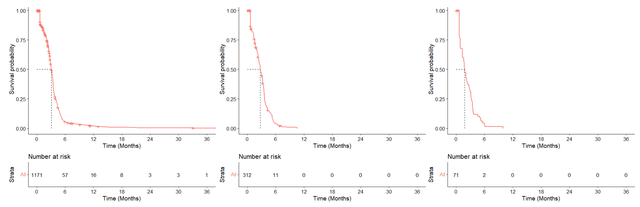
Abbreviations:1L; 1st line, 2L; 2nd line, 3L; 3rd line, SD; standard deviation)
Suppressed; numbers in any category with less that 10 patients cannot be reported due to confidentiality

Figure 4: Treatment patterns



Abbreviations: CAV; cyclophosphamide + doxorubicin + vincristine

Figure 5: Time-to-treatment discontinuation



Abbreviations:1L; 1st line, 2L; 2nd line, 3L; 3rd line, TTD, time-to-treatment discontinuation

- In 1L, most patients were treated with platinum + etoposide (83.7%), and use of the newly available PD-L1 inhibitors was limited because of the short period between their availability and study eligibility window.
- Of those initiating 2L, the vast majority were platinum sensitive; 247 (79.2%) had a CFI ≥ 180 days while only 65 patients (20.8%) had a CFI <180 days.
- Consequently, in 2L most patients were rechallenged with platinum + etoposide (58.7%) while a small proportion was treated with CAV(14.1%) and even smaller proportions treated with topotecan, Irinotecan (~5%) or other therapies.
- In 3L, patients were more evenly distributed across CAV (29.6%), platinum + etoposide (23.9%), and topotecan (19.7%).
- Median time to discontinuation reduced with each line (3.1 months, 2.8 months, and 1.8 months in 1L, 2L, and 3L respectively) (Figure 5).

Healthcare resource use

- While healthcare resource use was collected for up to 24 months of each line of therapy, patients were in each line for a much shorter period, with median follow up time of between 7.7 months, 6.1 months, and 4.0 months in lines 1, 2, and 3, respectively (Table 3).
- Non-cancer practitioner visits were the most utilized component of HCRU with a mean of 32.7, 28.9, and 22.0 visits per patient in 1L, 2L, and 3L, respectively.

Table 3: Healthcare resource use during each line of therapy for ES-SCLC

	1L (n =1,171)			2L (n = 312)			3L (n = 71)		
	Total	Mean per patient (SD)	Median	Total	Mean per patient (SD)	Median	Total	Mean per patient (SD)	Median
Follow-Up Time,(months)	10,832	9.3 (6.6)	7.7	2,298	7.4 (5.4)	6.1	384	5.4 (5.1)	4.0
Hospitalization	1,845	1.6 (1.4)	1.0	424	1.4 (1.3)	1.0	80	1.1 (1.1)	1.0
Emergency Ambulatory Visits	3,533	3.0 (3.7)	2.0	817	2.6 (3.5)	2.0	177	2.5 (4.0)	1.0
Non-Emergency Ambulatory Visits	5,357	4.6 (6.9)	2.0	1,161	3.7 (6.4)	2.0	173	2.4 (4.1)	1.0
Non-Cancer Practitioner Visits	38,283	32.7 (27.5)	26.0	9,019	28.9 (31.5)	21.0	1,564	22.0 (18.6)	17.0
Total	49,018	41.9 (32.3)	34.0	11,421	36.6 (34.6)	29.0	1,994	28.1 (21.2)	24.0

Abbreviations:1L; 1st line, 2L; 2nd line, 3L; 3rd line, SD; standard deviation
*The denominator is all patients in the line of therapy

Clinical outcomes

- Median rwOS was 7.8 months, 6.8 months, and 4.1 months in 1L, 2L, and 3L, respectively (Figure 6) .
- Median TTNT/D was 6.8 months, 5.5 months, and 3.9 months in 1L, 2L, and 3L, respectively (Figure 7).

Figure 6: Real-world overall survival by line of treatment

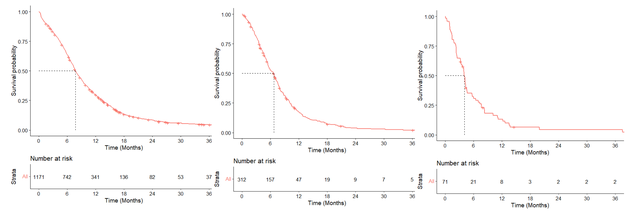
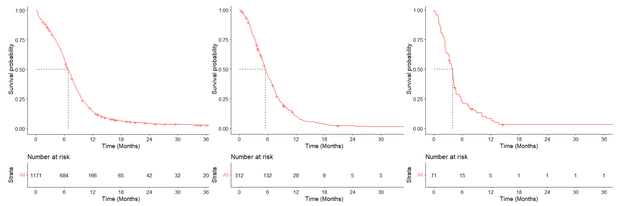


Figure 7: TTNT/D by line of treatment



Abbreviations:1L; 1st line, 2L; 2nd line, 3L; 3rd line, OS, overall survival, TTNT/D; time-to-next treatment or death

CONCLUSIONS

- **Treatment patterns were largely consistent with Canadian treatment guidelines, however the recent introduction of PD-L1 inhibitors was not fully reflected in 1L given the short period between their availability and study eligibility window [3,4].**
- **Systemic therapy for SCLC was associated with high attrition rates due to poor survival and a vast majority of patients did not make it past the 1st line of treatment where median rwOS was only 7.8 months.**
- **Total healthcare resource use in each line of treatment was substantial but decreased slightly with each line due to shorter treatment durations and survival in later lines.**
- **Clinical outcomes were poor and consistent with a previous study in Canada [8] suggesting persistently high unmet clinical need, particularly on progression from 1L treatment.**

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