BURDEN OF CHEMOTHERAPY-INDUCED MYELOSUPPRESSION AMONG PATIENTS WITH EXTENSIVE-STAGE SMALL CELL LUNG CANCER: A RETROSPECTIVE STUDY OF DATA FROM COMMUNITY ONCOLOGY PRACTICES

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INTRODUCTION

- Myelosuppression, which commonly manifests as neutropenia, anemia, thrombocytopenia, and/or lymphopenia, is a major dose-limiting complication of chemotherapy for patients with extensive-stage small cell lung cancer (ES-SCLC)[1–4]
  - Myelosuppression results from cytotoxic damage to hematopoietic stem and progenitor cells in the bone marrow, leading to reduced production of white blood cells, red blood cells, and/or platelets[1,3–5]
- Chemotherapy-induced myelosuppression places a substantial burden on patients and the health care system, owing to an increased risk of morbidity and mortality and of poor health-related quality of life[3–6]
- Management of myelosuppression often requires the administration of supportive care interventions such as growth factors and blood product transfusions, management of infectious complications, hospitalizations, and chemotherapy dose reductions and delays[3,7–9]

OBJECTIVE

- To describe treatment patterns, the burden of myelosuppression, and supportive care use among patients with ES-SCLC treated with chemotherapy in a US community oncology setting

METHODS

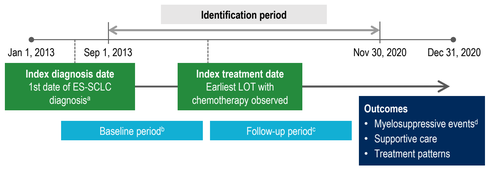
Study Design and Data Source

- This retrospective cohort study used electronic medical record (EMR) data from the Florida Cancer Specialists & Research Institute, a large community oncology/ hematology practice with nearly 70,000 new patients annually
- The study used data available between January 1, 2013, and December 31, 2020

Patient Population

- Adult patients (aged ≥ 18 years) with ES-SCLC who were treated with chemotherapy between September 1, 2013, and November 30, 2020, were identified. The date of the first chemotherapy-containing line of therapy (LOT) was defined as the index treatment date (**Figure 1**)
- Patients diagnosed with other primary tumors or enrolled in clinical trials during the study period were excluded
- Patients were followed up for a minimum of 30 days (unless the patient died) after the index treatment date until December 31, 2020, death, or end of activity in the EMR database

Figure 1. Study Design Overview



[a] Based on evidence of ES-SCLC diagnosis in the 180 days prior to the index treatment date for first LOT, or any time prior for second or later LOT. [b] Any time prior to the index treatment date. [c] ≥ 30 days after the index treatment date (patients who died in the first 30 days were included). [d] Anemia (grade 3: hemoglobin < 8.0 g/dL); neutropenia (grade 3: absolute neutrophil count [ANC] ≥ 500 to < 1000 cells/μL; grade 4: ANC < 500 cells/μL); thrombocytopenia (grade 3: ≥ 25,000 to < 50,000 platelets/μL; grade 4: < 25,000 platelets/μL); leukopenia (grade 3: ≥ 1,000 to < 2,000 white blood cells [WBC]/μL; grade 4: <1,000 WBC/μL); and lymphopenia (grade 3: ≥ 200 to < 500 lymphocytes/μL; grade 4: < 200 lymphocytes/μL). ES-SCLC, extensive-stage small cell lung cancer; LOT, line of therapy.

Outcomes and Analysis

- Incidence and frequency of myelosuppressive events/episodes (by type and grade), treatment patterns, and supportive care use (granulocyte colony-stimulating factor [G-CSF], erythropoiesis-stimulating agents [ESAs], and intravenous [IV] hydration) during the follow-up period were assessed
  - A myelosuppressive **event** was defined as each event on a unique date
    - Events were identified using laboratory values based on Common Terminology Criteria for Adverse Events version 5.0 definitions for neutropenia, anemia, thrombocytopenia, lymphopenia, and leukopenia (**Figure 1**)
  - A myelosuppressive **episode** was defined as all respective events occurring within 21 days of the first event, with the highest observed grade assigned to that episode
  - The following measures were reported for myelosuppression:
    - Rate and frequency of myelosuppressive episodes across all LOTs (main analysis)
    - Rate of myelosuppressive events across all LOTs and during the index LOT (sensitivity analysis)
- Eligibility to receive red blood cell (RBC) or platelet transfusions (hemoglobin [Hb] < 8 g/dL or platelets < 10,000/μL) was assessed
- Overall survival was assessed from the index treatment date

RESULTS

Demographic and Clinical Characteristics

- The study population included 1239 patients. Baseline demographic and clinical characteristics are summarized in **Table 1**
- Prior to chemotherapy initiation, the prevalence of myelosuppressive events was low, and very few patients had grade ≥ 3 events
  - In total, < 4% of patients had grade ≥ 3 neutropenia, < 2% had grade 3 anemia, and < 2% had grade ≥ 3 thrombocytopenia

Table 1. Baseline Demographics and Clinical Characteristics

Characteristic[a]	Patients with ES-SCLC (N = 1239)
Mean (SD) [median] age, years	66.9 (9.3) [68.0]
< 65 years, n (%)	462 (37.3)
≥ 65 years, n (%)	777 (62.7)
Male, n (%)	616 (49.7)
Race, n (%)	
White	719 (58.0)
Black	27 (2.2)
Asian	1 (0.1)
Other	441 (35.6)
Unknown	51 (4.1)
ECOG PS,[b,c] n (%)	
0	299 (24.1)
1	500 (40.4)
2	170 (13.7)
≥ 3	65 (5.2)
Mean (SD) non–cancer-related CCI	0.2 (0.5)
Non–cancer-related CCI, n (%)	
0	1116 (90.1)
1	77 (6.2)
≥ 2	46 (3.7)
Mean (SD) [median] follow-up duration from index treatment date, days	313 (338) [218]

[a] Measured any time prior to the index treatment date with the exception of ECOG PS and follow-up time. [b] 60 days before or 14 days after the index treatment date. [c] Unknown for 205 patients.
CCI, Charlson Comorbidity Index; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer.

Treatment Patterns

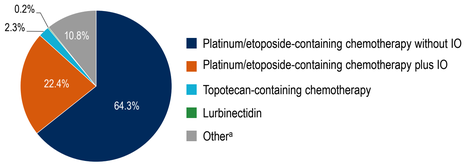
- Overall, 94.0% of patients started first-line chemotherapy at the index date (**Table 2**)
- Most patients (86.6%) received platinum/etoposide-containing chemotherapy (64.3% without other treatment, 22.4% in combination with immunotherapy) as the index regimen
- Following index treatment, 52.8% of patients received ≥ 1 subsequent LOT (**Table 2**; **Figure 2**)
- Patients received a median of 2 LOTs during the follow-up period

Table 2. Treatment Patterns During Follow-up

	Patients with ES-SCLC (N = 1239)
Index LOT, n (%)	
1	1165 (94.0)
2	71 (5.7)
≥ 3	3 (0.2)
Discontinued index LOT, n (%)	1172 (94.6)
Mean (SD) [median] time to discontinuation of index LOT, months	4.4 (4.9) [3.5]
Initiated next therapy, n (%)	654 (52.8)
Mean (SD) [median] time from start of index LOT to start of next LOT, months	6.2 (6.1) [4.6]
Mean (SD) [median] number of LOTs contributed during follow-up	1.9 (1.1) [2]
Number of LOTs contributed during follow-up, n (%)	
1	585 (47.2)
2	381 (30.8)
3	158 (12.8)
4	81 (6.5)
≥ 5	34 (2.7)

ES-SCLC, extensive-stage small cell lung cancer; LOT, line of therapy.

Figure 2. Index LOT Regimens

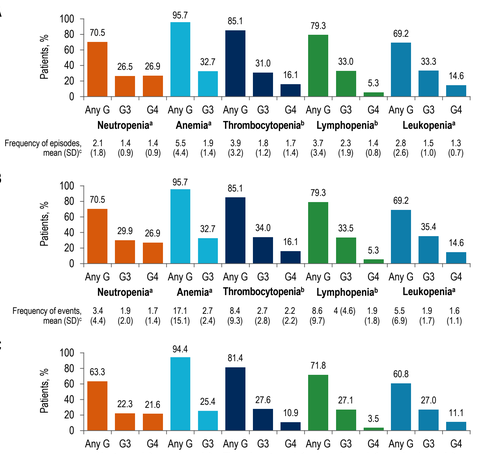


[a] Includes other chemotherapy agents alone (including a platinum-based agent without etoposide) or in combination with IO, chemotherapy plus other treatment, IO alone, and other treatment alone.
IO, immuno-oncology treatment; LOT, line of therapy.

Myelosuppressive Events

- During follow-up (mean ~10 months), 1222 (98.6%) patients had any myelosuppressive episode across all LOTs
  - 26.5% and 26.9% of patients had grade 3 and grade 4 neutropenia, respectively; 32.7% of patients had grade 3 anemia; and 31.0% and 16.1% of patients had grade 3 and grade 4 thrombocytopenia, respectively (**Figure 3A**)
    - 858 (69.5%) patients had grade ≥ 3 myelosuppressive episodes in ≥ 1 of the following: neutropenia, anemia, thrombocytopenia, lymphopenia, or leukopenia
  - The mean number of episodes was 1.4 for both grade 3 and grade 4 neutropenia, 1.9 for grade 3 anemia, 1.8 for grade 3 thrombocytopenia, and 1.7 for grade 4 thrombocytopenia (**Figure 3A**)

Figure 3. (A) Myelosuppressive Episodes Across All LOTs, (B) Myelosuppressive Events Across All LOTs, and (C) Myelosuppressive Events During the Index LOT



[a] n = 1236 patients with available laboratory data. [b] n = 1235 patients with available laboratory data.
[c] Among patients with ≥ 1 episode or event across all LOTs. [d] n = 1234 patients with available laboratory data.
G, grade; LOT, line of therapy.

- Consistent results were observed when comparing the prevalence of myelosuppressive events across all LOTs (**Figure 3B**) and during the index LOT (**Figure 3C**)
  - Nearly all patients had an any-grade myelosuppressive event, with anemia (all LOTs: 95.7%; index LOT: 94.4%) and thrombocytopenia (all LOTs: 85.1%; index LOTs: 81.4%) being the most common
- Overall, 20.6% of patients had both grade ≥ 3 neutropenia and grade 3 anemia, 21.5% of patients had grade 3 anemia and grade ≥ 3 thrombocytopenia, and 22.8% of patients had grade ≥ 3 neutropenia and grade ≥ 3 thrombocytopenia (**Figure 4**)

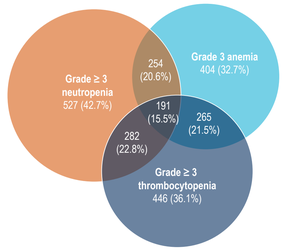
Supportive Care Use

- Overall, 32.6% of patients were eligible to receive RBC transfusions, 89.7% received G-CSF, 24.4% received ESAs, and 52.1% received IV hydration (**Table 3**)
- Among the 1112 patients who received G-CSF across all LOTs, 391 (35.2%) had grade 3 anemia and 435 (39.1%) had grade ≥ 3 thrombocytopenia
- Similarly, among the 302 patients who received ESAs, 175 (58.0%) had grade ≥ 3 neutropenia and 168 (55.6%) had grade ≥ 3 thrombocytopenia

Overall Survival

- 70.5% of patients died during follow-up; median (95% CI) overall survival was 9.2 (8.6–9.8) months

Figure 4. Grade ≥ 3 Myelosuppressive Episodes After Chemotherapy



767 (62.1%) patients had grade ≥ 3 myelosuppressive episodes in ≥ 1 lineage

419 (33.9%) patients had grade ≥ 3 myelosuppressive episodes in ≥ 2 lineages

191 (15.5%) patients had grade ≥ 3 myelosuppressive episodes in all 3 lineages

Data are n (%). Percentages were calculated using the total number of patients with laboratory data available for neutropenia, thrombocytopenia, and anemia (n = 1235) as the denominator.

Table 3. Use of Supportive Care Interventions

	Patients with ES-SCLC (N = 1239)
Patients eligible for transfusion, n (%)	418 (33.7)
RBC transfusion (Hb < 8 g/dL)	404 (32.6)
Platelet transfusion (platelets < 10,000/μL)	46 (3.7)
Patients receiving supportive care across all LOTs, n (%)	1165 (94.0)
G-CSF[a]	1112 (89.7)
Mean (SD) [median] G-CSF administrations[b] among all patients	5.7 (6.8) [4]
ESAs[c]	302 (24.4)
IV hydration	646 (52.1)

[a] Includes filgrastim (including biosimilars), tbo-filgrastim, pegfilgrastim (including biosimilars), and sargramostim.
[b] Count of unique administration days for G-CSF. [c] Includes epoetin alfa (and biosimilar).
ESA, erythropoiesis-stimulating agent; ES-SCLC, extensive-stage small cell lung cancer; G-CSF, granulocyte colony-stimulating factor; Hb, hemoglobin; IV, intravenous; LOT, line of therapy; RBC, red blood cell.

LIMITATIONS

- Inpatient data were not available
- Eligibility to receive RBC/platelet transfusions (Hb < 8 g/dL or platelets < 10,000/μL) was assessed because transfusion was not captured in the database
- Results from this study may not be generalizable beyond community oncology settings

CONCLUSIONS

- There is a high burden related to multilineage myelosuppression among chemotherapy-treated patients with ES-SCLC in the community oncology setting
  - A notable proportion of patients had myelosuppression in ≥ 2 lineages, suggesting an unmet need for managing the burden of multilineage myelosuppression among patients receiving single-lineage treatments
  - Close to 90% of patients received G-CSF, and more than half received IV hydration
- Therapies to protect bone marrow from myelosuppression could make treatment safer, reduce the need for supportive care, and potentially prevent the treatment of complications that may otherwise lead to the utilization of emergency departments and hospitalization

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