PATIENT CHARACTERISTICS ASSOCIATED WITH MYELOSUPPRESSION AMONG PATIENTS WITH EXTENSIVE-STAGE SMALL CELL LUNG CANCER TREATED WITH CHEMOTHERAPY IN THE COMMUNITY ONCOLOGY SETTING

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BACKGROUND

- Small cell lung cancer (SCLC) accounts for 13–17% of lung cancer diagnoses in the US,[1-3] with approximately two-thirds presenting with extensive-stage disease (ES-SCLC) at diagnosis[4,5]
- Chemotherapy has been the mainstay of treatment for ES-SCLC[2]
- Chemotherapy-induced myelosuppression (CIM) is a common complication of chemotherapy treatment among patients with advanced solid tumors, characterized by decreased bone marrow activity, resulting in anemia, neutropenia, and/or thrombocytopenia[5,6]
- Myelosuppression has a substantial impact on patients and healthcare systems[7,8]
- There is very limited research on whether there are risk factors associated with myelosuppression among patients with ES-SCLC

OBJECTIVE

- To examine the association between patient attributes and the risk of CIM in ES-SCLC, utilizing real-world data from US community oncology practices

METHODS

STUDY DESIGN AND DATA SOURCE

- This was a retrospective observational study using data from the US Oncology Network's iKnowMed (iKM) electronic health record system
- The index date was defined as the initiation of chemotherapy for ES-SCLC
- Patients were followed from index date through Dec 31, 2020, the date of last visit or date of death, whichever occurred earliest **(Figure 1)**

STUDY POPULATION

- Include patients age ≥18 years old with a diagnosis of ES-SCLC
- Exclude patients who were enrolled in clinical trials and those who received treatments for other primary tumors during the study period
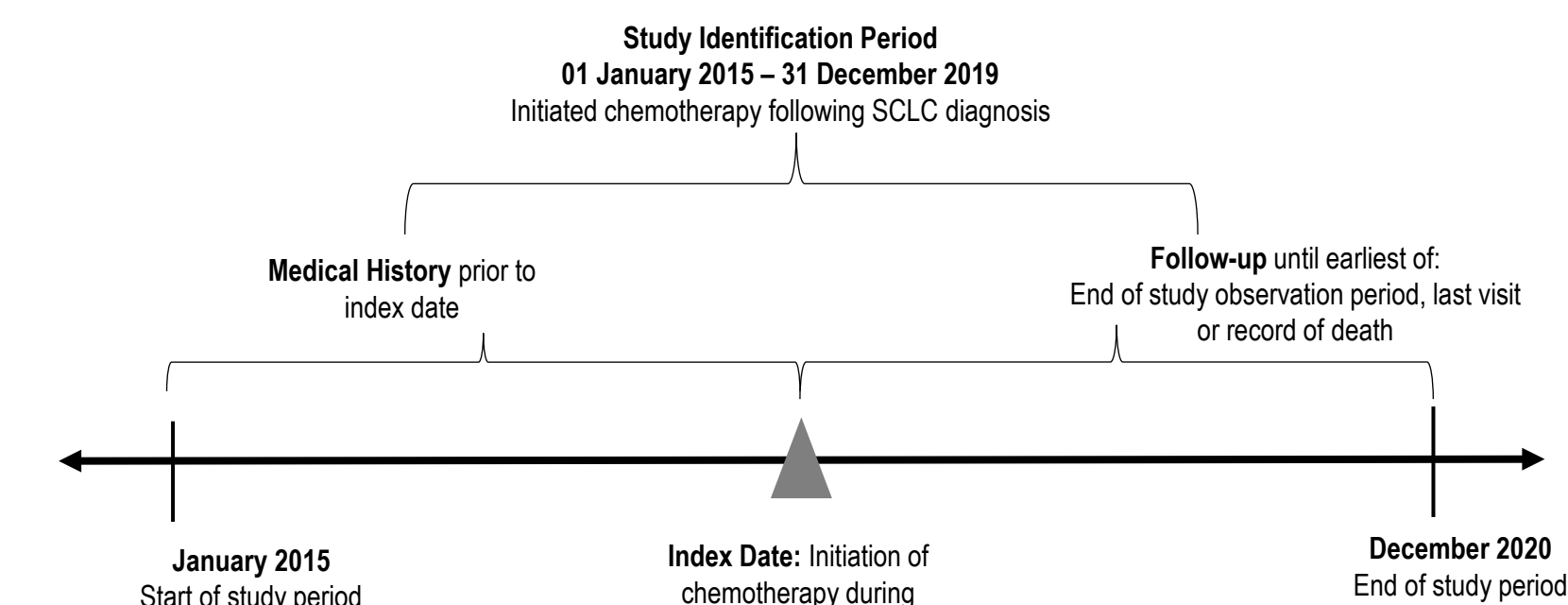
OUTCOMES AND ANALYSES

- Myelosuppression events were identified using laboratory values based on CTCAE v5.0 definitions for anemia, neutropenia, and thrombocytopenia
  - Grade ≥ 3 anemia: hemoglobin <8.0 g/dL
  - Grade ≥ 3 neutropenia: absolute neutrophil count <1,000/μL
  - Grade ≥ 3 thrombocytopenia: platelet count <50,000/μL
- Multivariate regression analyses were performed to examine the association between patient characteristics and the risk of experiencing a grade ≥3 myelosuppression in at least one lineage
  - Myelosuppression was coded as 1 if patients had any of the following post-chemotherapy initiation: grade ≥3 neutropenia, grade ≥3 anemia, grade ≥3 thrombocytopenia; as 0 if patients had none of the grade ≥3 cytopenia mentioned above post-chemotherapy initiation
- Sensitivity analyses were conducted on the risk of having a grade ≥3 myelosuppression for each lineage

CTCAE: Common Terminology Criteria for Adverse Events

- The areas under the receiver operating characteristic (ROC) curve (AUCs) were reported for all the regression models

Figure 1. Study Design Overview

Study Identification Period
01 January 2015 – 31 December 2019
Initiated chemotherapy following SCLC diagnosis

Medical History prior to index date

Follow-up until earliest of:
End of study observation period, last visit or record of death

January 2015 Start of study period

Index Date: Initiation of chemotherapy during study period

December 2020 End of study period

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

- A total of 1,574 adult patients with ES-SCLC receiving chemotherapy were included in the final sample
- Mean age 68 years, 82.2% White, 52.4% female, and 55.5% with an ECOG score ≤1) **(Table 1)**
- Follow up duration was an average of 8.9 months (SD: 8.5)

MYELOSUPPRESSION DURING FOLLOW-UP

- Grade ≥ 3 myelosuppression in at least 1 lineage occurred in 56.6% of patients in the overall population
  - Grade ≥ 3 anemia occurred in 28.5% of patients
  - Grade ≥ 3 neutropenia occurred in 35.7% of patients
  - Grade ≥ 3 thrombocytopenia occurred in 22.9% of patients

MULTIVARIATE LOGISTIC REGRESSION RESULTS

- Results from the main model on the risk of having a grade 3 or higher myelosuppression in at least one lineage **(Figure 2, Table 2)**
  - Patient demographics (age, sex, and race) and baseline labs for hemoglobin, absolute neutrophil count, and platelets were not identified as predictors
  - A higher dosage of chemotherapy was associated with an increased risk of having grade ≥ 3 myelosuppression
  - An index treatment hold, or delay, was associated with a higher risk of having grade ≥ 3 myelosuppression compared to those without a hold or delay
  - Prophylactic G-CSF use (defined as receiving G-CSF within 3 days of chemotherapy initiation) was associated with a lower risk of having grade ≥ 3 myelosuppression compared to those who did not receive prophylactic G-CSF
- Similar results were observed in the sensitivity analysis **(Figure 2, Table 2)**
- The AUC was 0.64 for the main model predicting grade 3 or higher myelosuppression in at least one lineage and was 0.70, 0.65, and 0.60 for the model predicting grade 3 or higher neutropenia, anemia, and thrombocytopenia respectively

G-CSF, granulocyte colony stimulating factor

Table 1: Demographic And Baseline Clinical Characteristics Among ES-SCLC Patients Receiving Chemotherapy

Characteristic	Patients (N=1,574)
Age at index, years, Mean (SD)	67.8 (9.1)
Female, n (%)	824 (52.4%)
Race, n (%)	
White	1,294 (82.2%)
Black	79 (5.0%)
Asian/Other	31 (2.0%)
Not documented	170 (10.8%)
ECOG performance status, n (%)	
0 or 1	874 (55.5%)
2 or 3	367 (23.3%)
Not documented	333 (21.2%)
Prophylactic G-CSF use, n (%)	691 (43.9%)
Average dose of index chemotherapy: Carboplatin (AUC)	4.7 (0.8)
Average dose of index chemotherapy: Cisplatin (mg/m²)	60.3 (24.9)
Average dose of index chemotherapy: Etoposide (mg/m²)	93.9 (11.7)
Index treatment hold, n (%) [a]	142 (9.2)
Index treatment delays, n (%) [b]	1,298 (84.5)
Hemoglobin during baseline, n (%) [c]	
Abnormal	816 (51.8)
Normal	483 (30.7)
Not documented	275 (17.5)
ANC during baseline, n (%) [d]	
Abnormal	150 (9.5)
Normal	1,027 (65.3)
Not documented	397 (25.2)
Platelet count during baseline, n (%) [e]	
Abnormal	266 (16.9)
Normal	1042 (66.2)
Not documented	266 (16.9)

Abbreviations: ANC, Absolute Neutrophil Count; AUC, area under curve; ECOG, Eastern Cooperative Oncology Group; ES-SCLC, extensive-stage small cell lung cancer; G-CSF, granulocyte colony-stimulating factor
[a]Treatment hold is defined as a gap of at least 60 days without treatment.
[b]Treatment delay is defined as a gap of 14-59 days without treatment.
[c]Abnormal hemoglobin defined as those who had grade 1 or higher anemia (hemoglobin < 13 g/dL)
[d]Abnormal ANC defined as those who had grade 1 or higher neutropenia (ANC < 2,500 /μL)
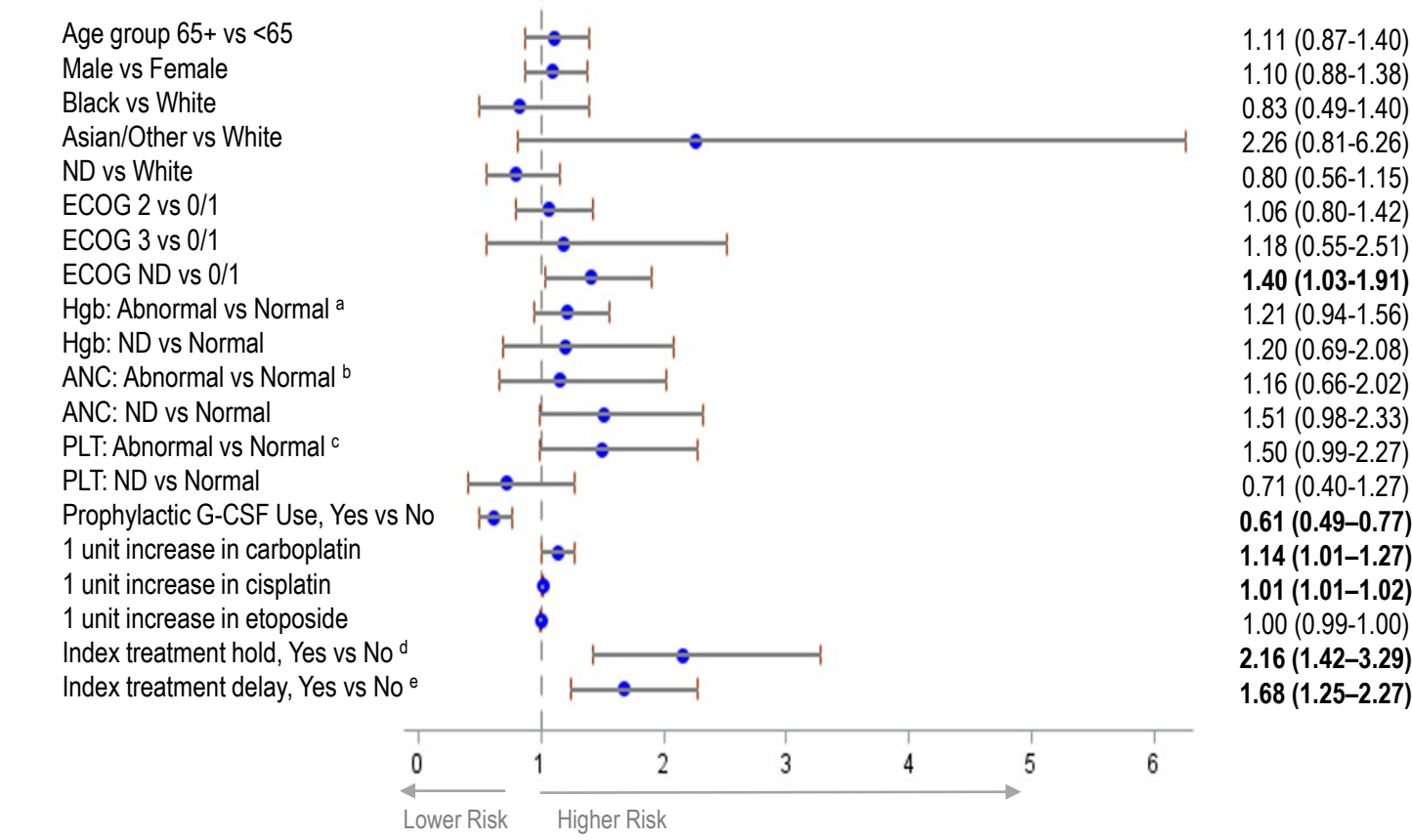[e]Abnormal platelet defined as those who had grade 1 or higher thrombocytopenia (platelet < 150,000 /μL)

Figure 2. Results From Multivariate Regression Models

2A. Regression model on the risk of having a grade ≥3 myelosuppression in at least one lineage

OR (95%CI)

	OR (95%CI)
Age group 65+ vs <65	1.11 (0.83-1.37)
Male vs Female	1.10 (0.88-1.38)
Black vs White	0.83 (0.49-1.40)
Asian/Other vs White	2.26 (0.81-6.26)
ND vs White	0.80 (0.56-1.15)
ECOG 2 vs 0/1	1.06 (0.80-1.42)
ECOG 3 vs 0/1	1.18 (0.55-2.51)
ECOG ND vs 0/1	1.40 (1.03-1.91)
Hgb: Abnormal vs Normal [a]	1.21 (0.94-1.56)
Hgb: ND vs Normal	1.20 (0.69-2.08)
ANC: Abnormal vs Normal [b]	1.16 (0.66-2.02)
ANC: ND vs Normal	1.51 (0.98-2.33)
PLT: Abnormal vs Normal [c]	1.50 (0.99-2.27)
PLT: ND vs Normal	0.71 (0.40-1.27)
Prophylactic G-CSF Use, Yes vs No	0.61 (0.49-0.77)
1 unit increase in carboplatin	1.14 (1.01-1.27)
1 unit increase in cisplatin	1.01 (1.01-1.02)
1 unit increase in etoposide	1.00 (0.99-1.00)
Index treatment hold, Yes vs No [d]	2.16 (1.42-3.29)
Index treatment delay, Yes vs No [e]	1.68 (1.25-2.27)

2B. Regression model on the risk of having a grade ≥3 neutropenia

	OR (95%CI)
Age group 65+ vs <65	1.07 (0.83-1.37)
Male vs Female	1.01 (0.79-1.29)
Black vs White	0.83 (0.47-1.47)
Asian/Other vs White	1.25 (0.50-3.12)
ND vs White	0.74 (0.50-1.16)
ECOG 2 vs 0/1	0.60 (0.44-0.83)
ECOG 3 vs 0/1	0.80 (0.35-1.84)
ECOG ND vs 0/1	0.72 (0.51-1.01)
ANC: Abnormal vs Normal [b]	1.36 (0.78-2.36)
ANC: ND vs Normal	0.78 (0.54-1.18)
Prophylactic G-CSF Use, Yes vs No	0.29 (0.22-0.37)
1 unit increase in carboplatin	1.16 (1.02-1.32)
1 unit increase in cisplatin	1.01 (1.01-1.02)
1 unit increase in etoposide	1.00 (0.99-1.00)
Index treatment hold, Yes vs No [d]	1.85 (1.23-2.78)
Index treatment delay, Yes vs No [e]	1.58 (1.17-2.15)

2C. Regression model on the risk of having a grade ≥3 anemia

	OR (95%CI)
Age group 65+ vs <65	1.12 (0.87-1.44)
Male vs Female	0.83 (0.65-1.06)
Black vs White	1.36 (0.82-2.27)
Asian/Other vs White	1.37 (0.61-3.07)
ND vs White	0.71 (0.46-1.09)
ECOG 2 vs 0/1	0.89 (0.64-1.26)
ECOG 3 vs 0/1	2.33 (1.08-5.03)
ECOG ND vs 0/1	1.69 (1.26-2.28)
Hgb: Abnormal vs Normal [a]	1.91 (1.44-2.53)
Hgb: ND vs Normal	0.90 (0.59-1.35)
1 unit increase in Carboplatin	1.11 (0.98-1.26)
1 unit increase in Cisplatin	1.01 (1.00-1.02)
1 unit increase in Etoposide	0.99 (0.99-1.00)
Index treatment hold, Yes vs No [d]	1.78 (1.22-2.62)
Index treatment delay, Yes vs No [e]	1.55 (1.15-2.08)

2D. Regression model on the risk of having a grade ≥3 thrombocytopenia

	OR (95%CI)
Age group 65+ vs <65	1.07 (0.81-1.40)
Male vs Female	1.04 (0.81-1.35)
Black vs White	0.50 (0.25-1.00)
Asian/Other vs White	0.86 (0.34-2.17)
ND vs White	0.99 (0.65-1.50)
ECOG 2 vs 0/1	1.11 (0.80-1.56)
ECOG 3 vs 0/1	1.54 (0.68-3.45)
ECOG ND vs 0/1	1.12 (0.81-1.57)
PLT: Abnormal vs Normal [c]	1.99 (1.33-2.98)
PLT: ND vs Normal	0.96 (0.65-1.42)
1 unit increase in carboplatin	1.08 (0.95-1.24)
1 unit increase in cisplatin	1.01 (1.00-1.02)
1 unit increase in etoposide	1.00 (0.99-1.01)
Index treatment hold, Yes vs No [d]	1.50 (1.00-2.25)
Index treatment delay, Yes vs No [e]	1.78 (1.31-2.43)

Abbreviations: ND, Not documented; ECOG, Eastern Cooperative Oncology Group; Hgb, Hemoglobin; ANC, Absolute Neutrophil Count; PLT, Platelet; G-CSF, granulocyte colony-stimulating factor
[a]Abnormal hemoglobin defined as those who had grade 1 or higher anemia (hemoglobin < 13 g/dL); [b]Abnormal ANC defined as those who had grade 1 or higher neutropenia (ANC < 2,500 /μL); [c]Abnormal platelet defined as those who had grade 1 or higher thrombocytopenia (platelet < 150,000 /μL); [d]Treatment hold is defined as a gap of at least 60 days without treatment. [e]Treatment delay is defined as a gap of 14-59 days without treatment.

Table 2. Summary Of Regression Results Among ES-SCLC Patients

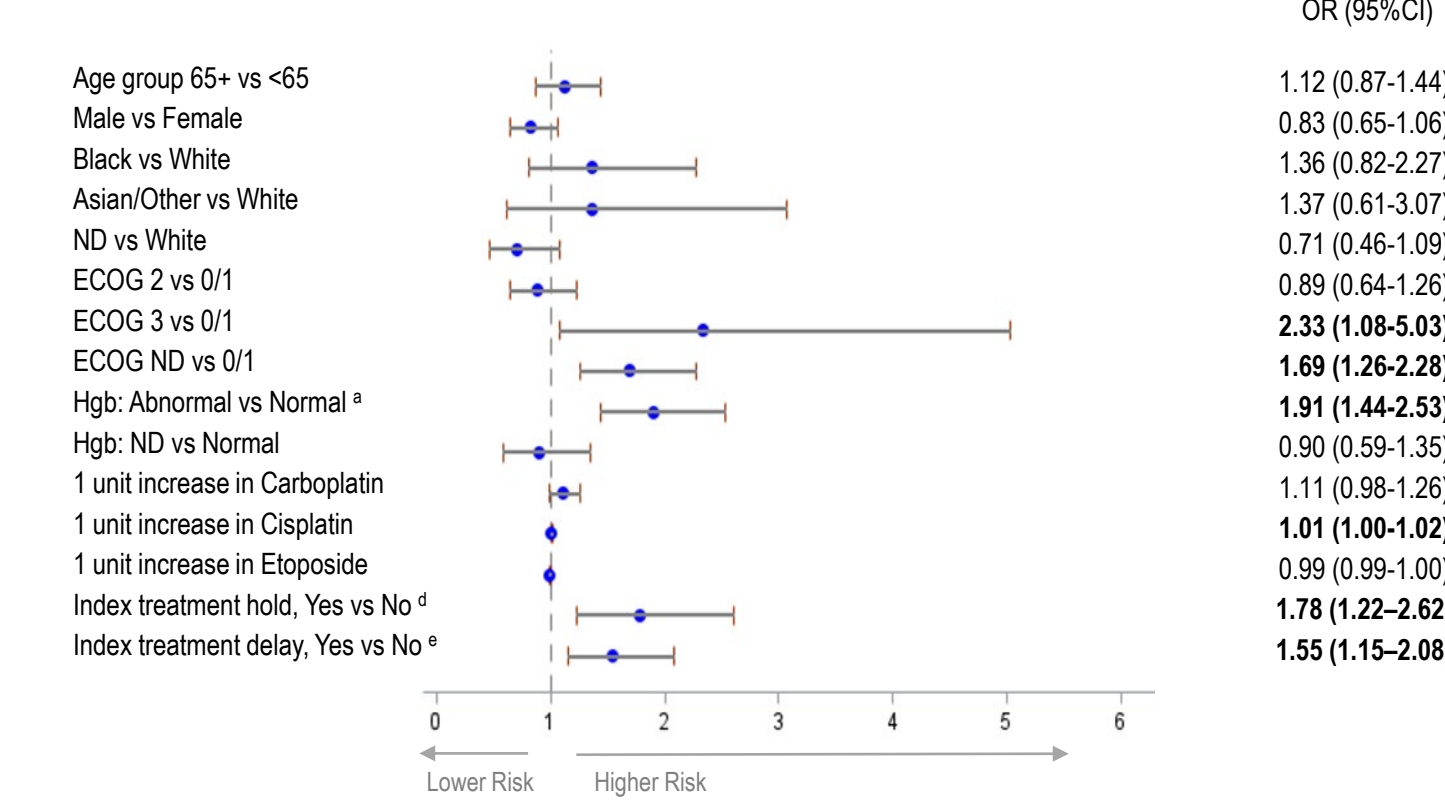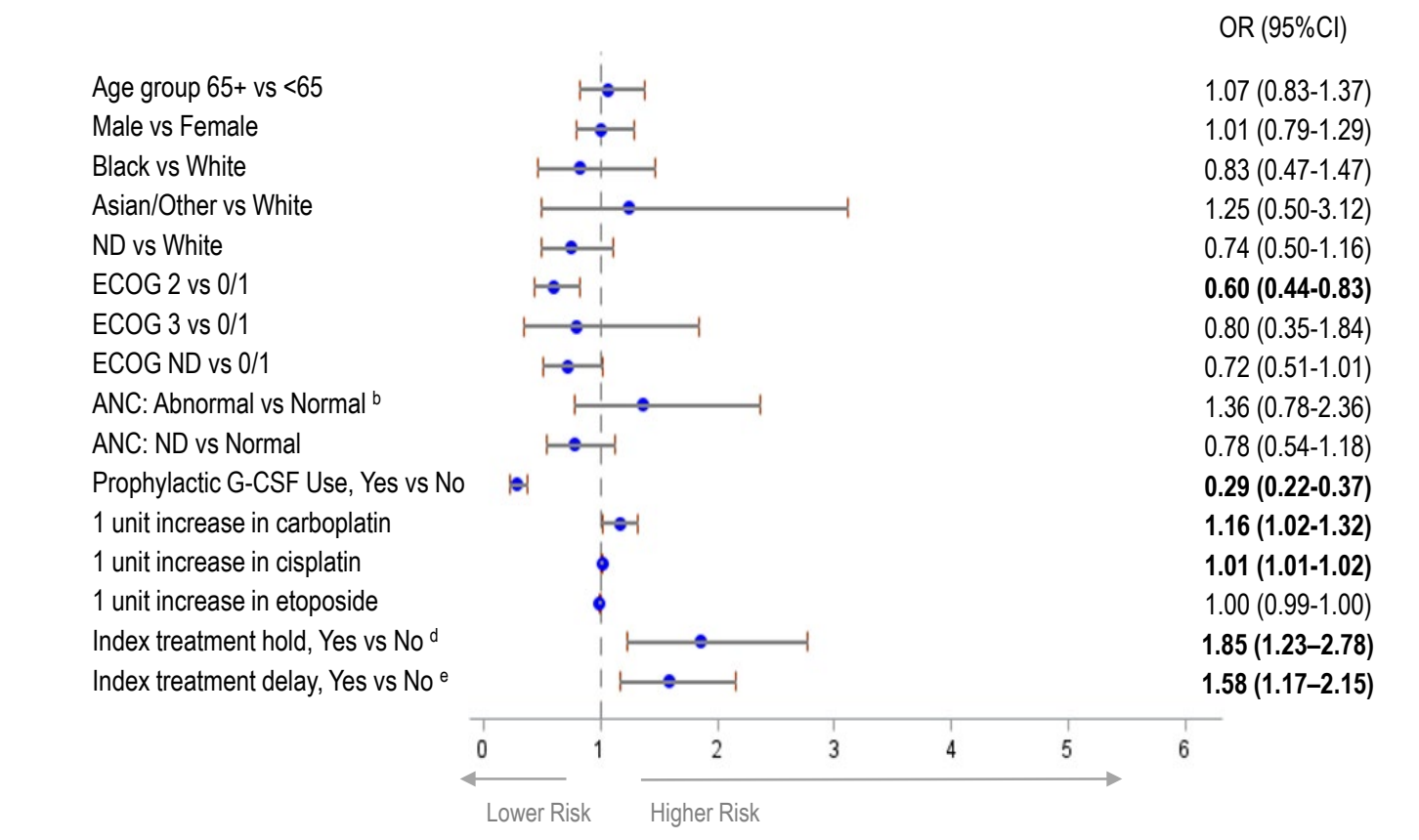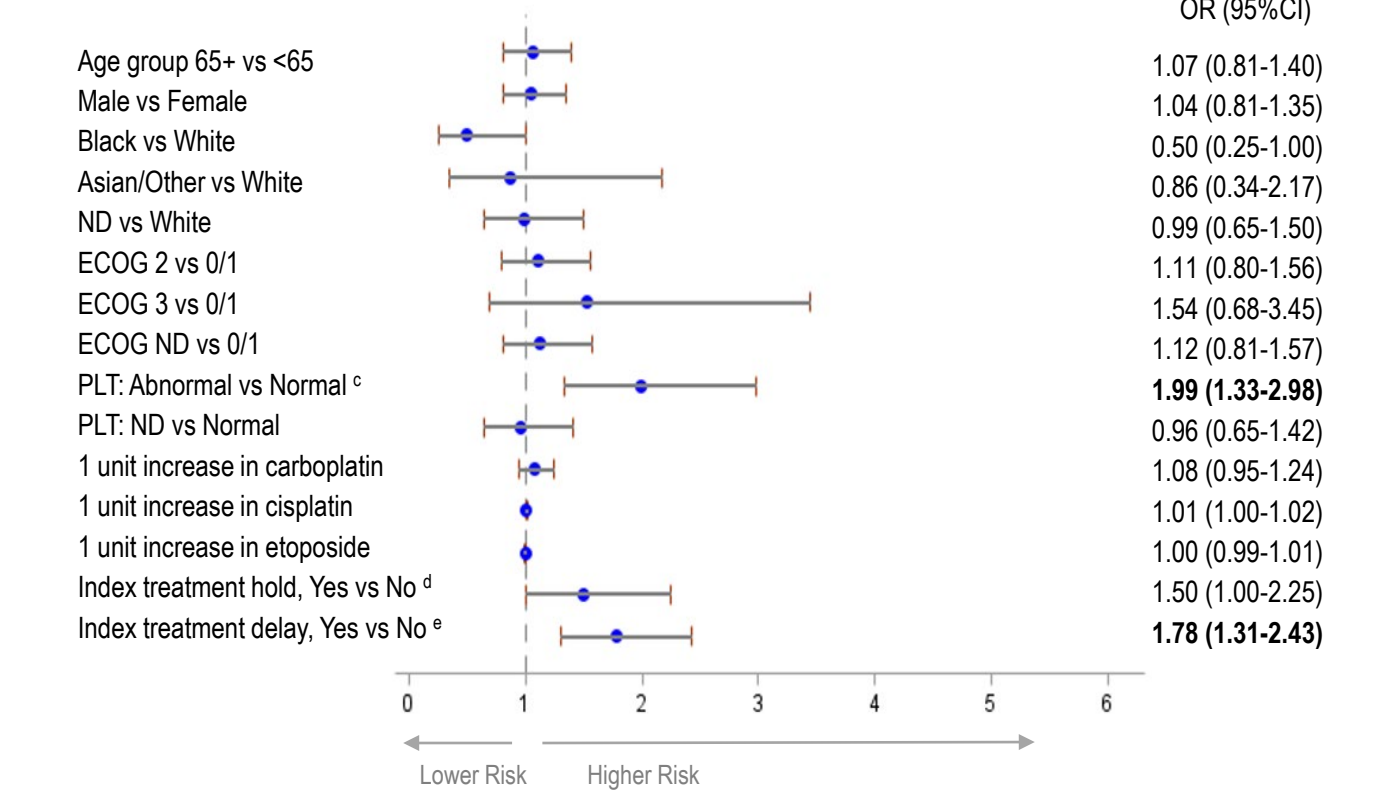|	Main model	Lineage-specific models (sensitivity analysis)		
	Risk of grade ≥3 myelosuppression in at least one lineage	Risk of grade ≥3 neutropenia	Risk of grade ≥3 anemia	Risk of grade ≥3 thrombocytopenia
Age, sex, race	No association			
ECOG	No association	ECOG 2 had lower than ECOG 0/1*	ECOG 3 had higher risk than ECOG 0/1	No association
Abnormal baseline hemoglobin	No association	Not included	Associated with higher risk	Not included
Abnormal baseline ANC	No association	No association	Not included	Not included
Abnormal baseline platelet	No association	Not included	Not included	Associated with higher risk
Prophylactic G-CSF use	Associated with lower risk	Associated with lower risk	Not included	Not included
Dose of index chemotherapy	Higher doses associated with higher risk	Higher doses associated with higher risk	Higher doses associated with higher risk	No association
Index treatment hold	Associated with higher risk	Associated with higher risk	Associated with higher risk	No association
Index treatment delay	Associated with higher risk	Associated with higher risk	Associated with higher risk	Associated with higher risk

*This may be explained by the fact that patients with higher ECOG score received less chemotherapy than those with ECOG 0/1 (chemotherapy duration approximately 2 months for ECOG 2/3 vs. 3 months for patients with ECOG 0/1)
Abbreviations: ANC: absolute neutrophil count; G-CSF: granulocyte colony stimulating factor; ECOG: Eastern Cooperative Oncology
No association: covariate was included in the multivariate model, but no statistically significant association was identified. Not included: variables relevant to the outcome of interest were included in the regression analysis; variables not relevant to the outcome of interest were not included in the regression analysis.

LIMITATIONS

- Study results may be limited in generalizability to other ES-SCLC patients in the US treated in a community oncology setting
- This study did not evaluate risk factors of CIM with lower grade (e.g., grade 1 or 2), which may impact patients' experience

CONCLUSIONS

- These results indicate patient characteristics are not risk factors for myelosuppressive events among patients with ES-SCLC receiving chemotherapy, and this finding suggests that how patients present in initial visits are not necessarily predictive of myelosuppressive events
- Further studies may be needed to confirm these findings

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