C0126

Competing Risks of Death in Older Adults with Advanced Non-Small Cell Lung Cancer Receiving Programmed Cell Death Protein 1 (PD-1) Inhibitors

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BACKGROUND

- Lung cancer remains the leading cause of cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) representing approximately 85%.[1]
- Understanding cardiovascular disease (CVD)-related deaths in NSCLC patients is important, as cardiovascular health significantly influences survival and treatment outcomes, particularly as cancer therapies can exacerbate underlying CVD risks.[2]
- Programmed Cell Death Protein 1 (PD-1) inhibitors, a breakthrough in immunotherapy for NSCLC, have been associated with cardiovascular events.[3]
- However, little is known about the factors associated with CVD mortality in patients with NSCLC, especially those treated with nivolumab and pembrolizumab.

OBJECTIVES

- To examine the competing risks of the cause of death among older patients with NSCLC receiving PD-1 inhibitors
- To identify factors influencing CVD and NSCLC mortality
- To understand the differences of mortalities between two PD-1 inhibitors

METHODS

Data Source

- The 2006-2019 Surveillance, Epidemiology, and End Results (SEER) - Medicare linked database

Study Design

- Retrospective cohort study

Study Population

- Aged 65 years or older
- Diagnosed with advanced (stage IIIB-IV) NSCLC
- Treated with pembrolizumab or nivolumab

Outcome

- Four types of mortality
  : (1) CVD; (2) NSCLC; (3) other cancers; (4) other diseases

Key Variables

- Demographics: age, sex, race
- Cancer-related factors: cancer stage, histology
- Socioeconomic status: region, primary insurance provider
- Clinical characteristics: smoking history, obesity, comorbidities.

Statistical Analysis

- Descriptive analysis
  : independent t-test (Fisher's exact test), chi-square test
- Competing risk models
  - when multiple potential events could preclude the event of interest, to assess CVD or NSCLC mortality and associated factors
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RESULTS

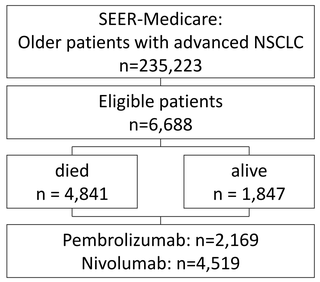

Figure 1. Patient selection

Table 1. Patient characteristics

	Pembrolizumab (n=2,169)	Nivolumab (n=4,519)	P-value
Sex, n (%)			
Male	1,047 (48.27)	2,304 (50.98)	0.0391
Female	1,122 (51.73	2,215 (49.02)	
Age group, n (%)			
65-69	282 (13)	606 (13.41)	
70-74	576 (26.56)	1,340 (29.65)	0.0346
75-79	661 (30.47)	1,326 (29.34)	
80+	650 (29.97)	1,247 (27.59)	
Race, n (%)			
Non-Hispanic White	1,826 (84.19)	3,608 (79.84)	
Non-Hispanic Black	125 (5.76)	356 (7.88)	0.0003
Hispanic	87 (4.01)	299 (5.07)	
Others	131 (6.04)	326 (7.21)	
Stage, n (%)			
Stage IIIB or regional	503 (23.19)	1,403 (31.05)	<0.0001
Stage IV or distant	1,666 (76.81)	3,116 (68.95)	
CCI, n (%)			
CCI = 0	34 (1.57)	80 (1.77)	0.7904
0 < CCI < 9	873 (40.25)	1,796 (39.74)	
9 ≤ CCI	1,262 (58.18)	2,643 (58.49)	

Table 2. Distribution of cause of mortality

	Cause of death			
	CVD	NSCLC	Other cancer	Other disease
Nivolumab	100 (2.81%)	3,052 (85.75%)	245 (6.88%)	162 (4.55%)
Pembrolizumab	51 (3.98%)	1,047 (81.67%)	101 (7.88%)	83 (6.47%)

Variables	Pembrolizumab Events/N (%)		Nivolumab Events/N (%)		HR (95% CI)
Sex					
Male	1047/2169	(48.3)	2304/4519	(51.0)	0.95 (0.59, 1.51)
Female	1122/2169	(51.7)	2215/4519	(49.0)	0.86 (0.53, 1.38)
Age level					
65-69	282/2169	(13.0)	606/4519	(13.4)	0.95 (0.59, 1.51)
70-74	576/2169	(26.6)	1340/4519	(29.7)	0.88 (0.56, 1.39)
75-79	661/2169	(30.5)	1326/4519	(29.3)	0.83 (0.53, 1.30)
80+	650/2169	(30.0)	1247/4519	(27.6)	0.88 (0.57, 1.37)
Race					
NH-White	1826/2169	(84.2)	3608/4519	(79.8)	0.95 (0.59, 1.51)
NH-Black	125/2169	(5.8)	356/4519	(7.9)	0.80 (0.48, 1.33)
Hispanic	87/2169	(4.0)	229/4519	(5.1)	0.81 (0.47, 1.40)
Others	131/2169	(6.0)	326/4519	(7.2)	1.04 (0.63, 1.72)
Stage					
Stage IIIB or Regional	503/2169	(23.2)	1403/4519	(31.0)	0.95 (0.59, 1.51)
Stage IV or Distant	1666/2169	(76.8)	3116/4519	(69.0)	1.01 (0.64, 1.57)
Histology					
Squamous	375/2169	(17.3)	1384/4519	(30.6)	0.95 (0.59, 1.51)
Adenocarcinoma	1641/2169	(75.7)	2858/4519	(63.2)	0.73 (0.46, 1.16)
Large/Others	153/2169	(7.1)	277/4519	(6.1)	0.86 (0.52, 1.43)
Radiation					
Yes	801/2169	(36.9)	1982/4519	(43.9)	1.20 (0.76, 1.90)
Surgery					
Yes	198/2169	(9.1)	564/4519	(12.5)	0.72 (0.44, 1.16)
Smoking					
Yes	1369/2169	(63.1)	2725/4519	(60.3)	1.06 (0.66, 1.69)
CHF					
Yes	399/2169	(18.4)	958/4519	(21.2)	1.26 (0.77, 2.06)
COPD					
Yes	1404/2169	(64.7)	3093/4519	(68.4)	1.02 (0.65, 1.62)
Mild liver disease					
Yes	397/2169	(18.3)	1024/4519	(22.7)	0.84 (0.51, 1.38)
Plegia					
Yes	65/2169	(3.0)	94/4519	(2.1)	1.49 (0.80, 2.74)

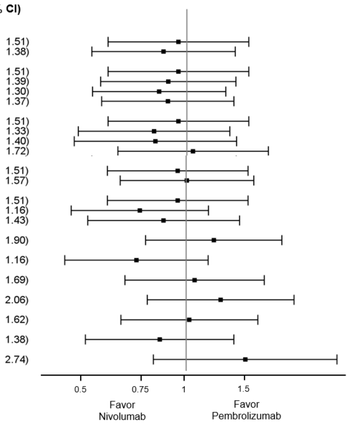

Figure 2. Hazard ratios of all-cause death with factors in the multivariable Cox model

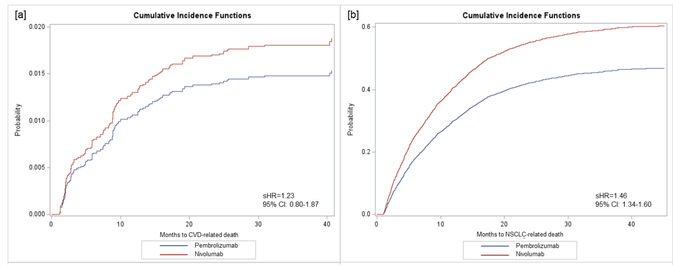

Figure 3.
CIF curves: Fine-Gray model
[a] CVD mortality;
[b] NSCLC mortality

Table 3. Key factors of each mortality considering competing risk: Fine-Gray model

	Sub-distribution hazard ratios by cause of death			
	CVD	NSCLC	Other cancer	Other disease
Age group				
65-69	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
70-74	1.75 (0.85-3.61)	1.03 (0.93-1.15)	0.79 (0.57-1.10)	1.34 (0.84-2.13)
75-79	2.18 (1.07-4.46)	1.14 (1.03-1.27)	0.80 (0.58-1.11)	1.35 (0.85-2.14)
80+	2.34 (1.16-4.73)	1.21 (1.09-1.35)	0.73 (0.55-1.03)	1.31 (0.83-2.09)
Cognitive heart failure				
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	2.36 (1.68-3.31)	1.08 (1.00-1.17)	0.85 (0.64-1.12)	2.18 (1.66-2.86)
Chronic obstructive pulmonary disease				
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	0.91 (0.62-1.34)	1.06 (0.99-1.14)	1.09 (0.85-1.40)	1.16 (0.86-1.57)

METHODS (Cont'd)

Statistical Analysis

- **The Fine-Gray model**: to estimate the cumulative incidence of an event in the presence of competing risks
- **Cause-specific Cox regression model:** to understand relationships between covariates and the risk of a specific type of event

REFERENCES

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CONCLUSIONS

Key takeaways

- There was no significant difference in CVD-related mortality between the two PD-1 inhibitors.
- Older age and a history of heart failure were found to be at a higher risk for CVD and NSCLC-related death.

Strengths

- The SEER-Medicare linked database enabled a large population-based analysis.
- This study provides a better understanding of the factors affecting four types of mortalities, suggesting the importance of managing CVD comorbidities in NSCLC patients.

[Acknowledgement]

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