Appendix 1

Methods

Line of treatment determination

In this study, beginning of first-line treatment was defined as initiation of any systemic treatment (including ICI monotherapy, ICI-chemotherapy combination or chemotherapy only) within 21 days from the onset of initial systemic treatment from diagnosis. Second-line therapy was deemed to have started when a distinct drug or regimen, not part of the first-line treatment, was initiated after day 21. Similarly, treatment was considered as third-line when different drug or regimen which was not a part of second line treatment was started after 21 days. Following criteria were not considered as start of a new drug or regimen:

- Cisplatin was substituted for carboplatin (or vice-versa).
- Paclitaxel was substituted for docetaxel or nab-paclitaxel (or vice-versa).
- Regimen that contained pemetrexed followed by continued administration of only pemetrexed.

Imputation of lung cancer diagnosis date

Given that SEER only provides the month and year of diagnosis, determining the exact day of lung cancer diagnosis required cross-referencing with the date of the initial medical claim indicating a lung cancer diagnosis (ICD-9/10-CM code: 162.x/C34.x). We compared this date to the month and year provided in SEER. We found a concordance rate of 78.8%, consistent with the 72.2% reported on the SEER-Medicare website (50). In cases where the month and year aligned between the two datasets, we utilized the date of the first claim with lung cancer diagnosis as the diagnosis date. For instances where there was a discrepancy in the month and year of diagnosis, we opted to impute the diagnosis date as the first day of the month reported in SEER.

Proxy performance status (PS) score

The proxy PS was computed by identifying healthcare services significantly associated with a poor disability status. Subsequently, a predicted probability of PS was determined using the beta coefficients from regression models published by Davidoff *et al.* [2014] (39). Applying a cut-off value of 0.115 recommended in the study, patients who had a predicted probability below the cut-off were classified as having a good PS (ECOG PS 0–2) and those with predicted probability of greater than or equal to the cut-off were classified as having poor PS (ECOG ≥3) (39,40,51).

References

50. SEER-Medicare: Defining the Date of Diagnosis & Treatment. Accessed January 2, 2022. Available online: https://healthcaredelivery.cancer.gov/seermedicare/considerations/date.html
51. ECOG-ACRIN Cancer Research Group. ECOG Performance Status Scale. Accessed May 5, 2022. Available online: https://ecog-acrin.org/resources/ecog-performance-status

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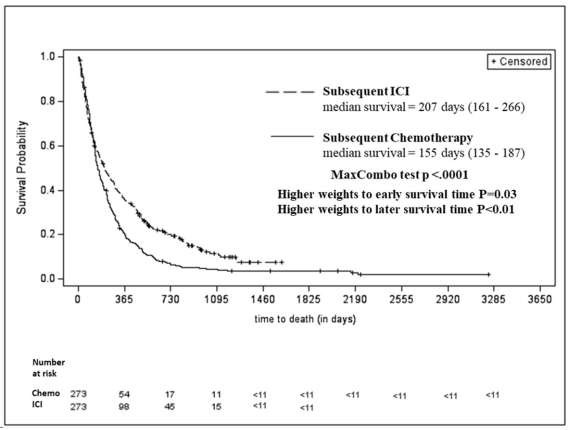

Figure S1 Kaplan-Meier survival curves of subsequent ICI *vs.* chemotherapy using MaxCombo test. All P values are significant at α <0.05. Per the SEER-Medicare data use agreement, count of <11 have been masked. Chemo, chemotherapy; ICI, immune checkpoint inhibitor.

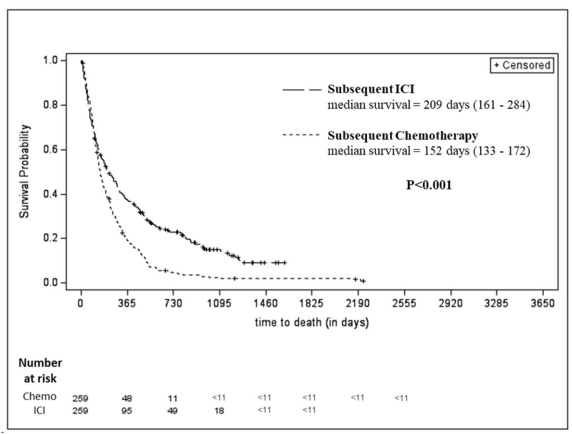

Figure S2 Kaplan-Meier survival curves of subsequent ICI *vs.* chemotherapy after propensity matching. All P values are significant at α <0.05. Per the SEER-Medicare data use agreement, count of <11 have been masked. Chemo, chemotherapy; ICI, immune checkpoint inhibitor.

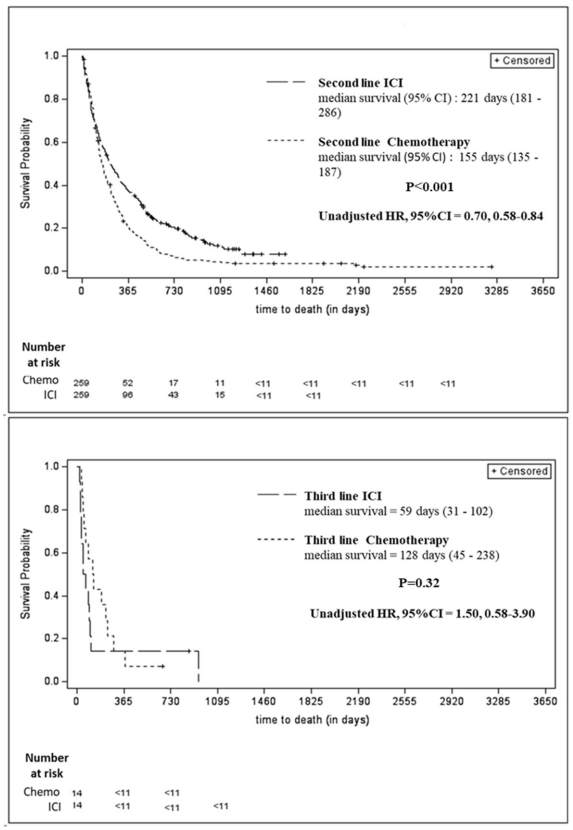

Figure S3 Kaplan-Meier survival curves by lines of subsequent treatment; top: second-line ICI *vs.* second-line chemotherapy; bottom: third-line ICI *vs.* third-line chemotherapy. All P values are significant at α <0.05. Per the SEER-Medicare data use agreement, count of <11 have been masked. Chemo, chemotherapy; ICI, immune checkpoint inhibitor; HR, hazard ratio; CI, confidence interval.

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Table S1 Adjusted hazard ratios of overall survival from multivariate Cox's proportional hazards regression analysis using shared frailty model with a random effect

Variables	HR (95% CI)	P value
Subsequent ICI *vs.* chemotherapy	0.62 (0.51–0.75)	<0.001
Age	1.03 (1.01–1.05)	0.008
Married *vs.* non-married	1.13 (0.92–1.38)	0.23
Female *vs.* male	0.87 (0.72–1.06)	0.16
Race		
Black *vs.* White	0.85 (0.59–1.22)	0.37
Other *vs.* White	0.82 (0.54–1.26)	0.37
Hispanic *vs.* non-Hispanic	1.09 (0.70–1.71)	0.70
Census tract poverty indicator level		
5–<10% *vs.* 0–<5%	1.28 (0.99–1.67)	0.06
10–<20% *vs.* 0–<5%	1.08 (0.82–1.43)	0.57
20–100% *vs.* 0–<5%	1.22 (0.86–1.72)	0.27
Unknown *vs.* 0–<5%	1.05 (0.71–1.55)	0.81
Non-metropolitan area *vs.* metropolitan area	0.88 (0.67–1.17)	0.39
Bone metastasis *vs.* no bone metastasis	1.27 (1.03–1.56)	0.02
Liver metastasis *vs.* no liver metastasis	1.61 (1.23–2.11)	<0.001
Lung metastasis *vs.* no lung metastasis	1.24 (0.99–1.54)	0.05
Charlson comorbidity index		
1 *vs.* 0	1.35 (1.07–1.70)	0.01
≥2 *vs.* 0	1.23 (0.94–1.60)	0.13
ECOG PS proxy 3–4 *vs.* ECOG PS proxy 0–2	1.21 (0.73–2.01)	0.45
Primary tumor grade		
Poorly differentiated/undifferentiated *vs.* well/moderately differentiated	1.07 (0.78–1.46)	0.67
Not determined *vs.* well/moderately differentiated	1.11 (0.83–1.48)	0.49
NSCLC histology		
Squamous cell *vs.* adenocarcinoma	1.84 (1.38–2.46)	<0.001
Other type *vs.* adenocarcinoma	1.06 (0.84–1.33)	0.64
Primary tumor size		
30 to <50 *vs.* <30 mm	1.13 (0.87–1.48)	0.36
50 to <70 *vs.* <30 mm	1.03 (0.76–1.39)	0.86
≥70 *vs.* <30 mm	1.34 (0.96–1.86)	0.08
Missing *vs.* <30 mm	0.95 (0.68–1.34)	0.77
Neurosurgical resection within 1 year of diagnosis (yes *vs.* no)	0.82 (0.62–1.07)	0.14
Cranial radiation before index treatment (no *vs.* yes)	0.63 (0.37–1.05)	0.07

HR, hazard ratio; CI, confidence interval; ICI, immune checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer.

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Table S2 Adjusted hazard ratios of overall survival from multivariate Cox's proportional hazards regression analysis using robust sandwich method with a change point of 114 days

Variables	HR (95% CI)	P value
Subsequent ICI *vs.* subsequent chemotherapy before 114 days change point	1.48 (1.09–2.02)	<0.001
Subsequent ICI *vs.* subsequent chemotherapy after 114 days change point	0.53 (0.42–0.68)	<0.001
Age	1.01 (0.99–1.03)	0.19
Married *vs.* non-married	0.99 (0.82–1.19)	0.87
Female *vs.* male	0.89 (0.74–1.06)	0.18
Race		
Black *vs.* White	1.11 (0.79–1.56)	0.56
Other *vs.* White	1.07 (0.74–1.55)	0.71
Hispanic *vs.* non-Hispanic	1.17 (0.77–1.78)	0.46
Census tract poverty indicator level		
5–<10% *vs.* 0–<5%	1.10 (0.85–1.40)	0.47
10–<20% *vs.* 0–<5%	0.94 (0.73–1.22)	0.64
20–100% *vs.* 0–<5%	0.90 (0.65–1.24)	0.51
Unknown *vs.* 0–<5%	0.89 (0.61–1.30)	0.54
Non-metropolitan area *vs.* metropolitan area	1.13 (0.86–1.50)	0.38
Bone metastasis *vs.* no bone metastasis	1.12 (0.94–1.33)	0.19
Liver metastasis *vs.* no liver metastasis	1.09 (0.85–1.40)	0.50
Lung metastasis *vs.* no lung metastasis	1.08 (0.86–1.34)	0.50
Charlson comorbidity index		
1 *vs.* 0	1.23 (0.98–1.55)	0.06
≥2 *vs.* 0	1.14 (0.91–1.41)	0.25
ECOG PS proxy 3–4 *vs.* ECOG PS proxy 0–2	1.39 (0.91–2.13)	0.13
Primary tumor grade		
Poorly differentiated/undifferentiated *vs.* well/moderately differentiated	1.03 (0.76–1.40)	0.83
Not determined *vs.* well/moderately differentiated	1.18 (0.87–1.59)	0.28
NSCLC histology		
Squamous cell *vs.* adenocarcinoma	1.06 (0.82–1.36)	0.67
Other type *vs.* adenocarcinoma	0.96 (0.77–1.20)	0.70
Primary tumor size		
>30 to <50 *vs.* <30 mm	1.13 (0.87–1.46)	0.35
>50 to <70 *vs.* <30 mm	1.14 (0.86–1.53)	0.36
≥70 *vs.* <30 mm	1.09 (0.76–1.57)	0.63
Missing *vs.* <30 mm	1.16 (0.85–1.59)	0.28
Neurosurgical resection within 1 year of diagnosis (yes *vs.* no)	0.92 (0.69–1.22)	0.56
Cranial radiation before index treatment (no *vs.* yes)	0.88 (0.56–1.37)	0.57

HR, hazard ratio; CI, confidence interval; ICI, immune checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer.

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Table S3 Standardized mean differences between cohorts before and after propensity score matching

Variables	Standardized mean differences (ICI-chemotherapy)			
	Before matching (n=716)		After matching (n=518)	
	Mean difference	Standardized difference	Mean difference	Standardized difference
Logit propensity score	0.52	0.72	0.06	0.09
Age	0.59	0.12	0.14	0.03
Days from diagnosis till index date	105.79	0.42	3.45	0.01
Male *vs.* female	0.01	0.01	0.00	0.01
Race				
White	0.01	0.02	0.00	–0.01
Black	0.03	0.11	0.01	0.04
Others	–0.04	–0.17	–0.01	–0.03
Hispanic	0.04	0.18	0.00	0.00
Married	–0.02	–0.04	0.02	0.03
Census tract poverty indicator level				
0–<5%	–0.06	–0.14	0.00	0.00
5–<10%	–0.01	–0.03	–0.02	–0.04
10–<20%	0.02	0.04	0.00	–0.01
20–100%	0.05	0.15	0.01	0.03
Unknown	0.00	0.02	0.01	0.05
Non-metropolitan area *vs.* metropolitan area	0.07	0.20	0.00	0.00
Lung metastasis at diagnosis	–0.01	–0.02	–0.01	–0.03
Bone metastasis at diagnosis	–0.04	–0.10	0.00	0.01
Liver metastasis at diagnosis	–0.04	–0.12	–0.01	–0.03
Charlson comorbidity index				
0	0.03	0.06	0.00	0.00
1	–0.01	–0.01	–0.01	–0.01
≥2	–0.02	–0.05	0.01	0.02
ECOG PS proxy 3–4 *vs.* ECOG PS proxy 0–2	0.01	0.05	0.02	0.08
NSCLC histology				
Adenocarcinoma	–0.05	–0.10	0.00	–0.01
Squamous cell	–0.03	–0.07	0.00	0.00
Other	0.07	0.17	0.00	0.01
Primary tumor size				
<30 mm	–0.01	–0.03	–0.02	–0.04
30 to <50 mm	0.00	–0.01	0.01	0.03
50 to <70 mm	0.00	0.01	0.01	0.03
≥70 mm	0.01	0.02	0.00	0.00
Missing	0.00	0.01	–0.01	–0.03
Primary tumor grade				
Well/moderately differentiated	0.02	0.05	0.00	0.00
Poorly differentiated/undifferentiated	0.01	0.01	0.01	0.01
Not determined	–0.02	–0.04	–0.01	–0.01
Cranial radiation before index treatment	0.00	0.01	0.01	0.01
Neurosurgical resection within 1 year of diagnosis	–0.03	–0.07	–0.01	–0.03
Line of treatment				
2nd line	–0.04	–0.10	–0.02	–0.05
3rd line	0.04	0.13	0.01	0.04
4th line	–0.01	–0.04	0.00	0.02

ICI, immune checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer.

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Table S4 Adjusted hazard ratios of overall survival from multivariate Cox proportional hazards regression analysis using sandwich method excluding those who did not receive cranial radiation prior to subsequent treatment

Variables	HR (95% CI)	P value
Subsequent ICI *vs.* subsequent chemotherapy	0.65 (0.51–0.82)	<0.01
Age	1.03 (1.00–1.06)	0.02
Married *vs.* non-married	1.30 (1.00–1.69)	0.04
Male *vs.* female	0.88 (0.71–1.11)	0.28
Race		
Black *vs.* White	0.96 (0.63–1.44)	0.82
Other *vs.* White	0.84 (0.52–1.34)	0.45
Hispanic *vs.* non-Hispanic	1.02 (0.61–1.70)	0.93
Census tract poverty indicator level		
5–<10% *vs.* 0–<5%	1.20 (0.88–1.66)	0.25
10–<20% *vs.* 0–<5%	1.05 (0.75–1.47)	0.79
20–100% *vs.* 0–<5%	1.15 (0.77–1.73)	0.49
Unknown *vs.* 0–<5%	1.02 (0.65–1.60)	0.93
Non-metropolitan area *vs.* metropolitan area	0.85 (0.58–1.24)	0.38
Bone metastasis *vs.* no bone metastasis	1.20 (0.92–1.55)	0.17
Liver metastasis *vs.* no liver metastasis	1.38 (0.94–2.03)	0.09
Lung metastasis *vs.* no lung metastasis	1.19 (0.90–1.58)	0.22
Charlson comorbidity index		
1 *vs.* 0	1.29 (0.94–1.77)	0.11
≥2 *vs.* 0	1.25 (0.95–1.65)	0.11
ECOG PS proxy 3-4 *vs.* ECOG PS proxy 0-2	1.11 (0.62–2.00)	0.72
Primary tumor grade		
Poorly differentiated/undifferentiated *vs.* well/moderately differentiated	1.23 (0.85–1.77)	0.27
Not determined *vs.* well/moderately differentiated	1.25 (0.89–1.76)	0.19
NSCLC histology		
Squamous cell *vs.* adenocarcinoma	2.00 (1.40–2.86)	<0.01
Other type *vs.* adenocarcinoma	1.02 (0.77–1.35)	0.88
Primary tumor size		
30 to <50 *vs.* <30 mm	1.23 (0.93–1.63)	0.14
50 to <70 *vs.* <30 mm	1.02 (0.69–1.51)	0.90
≥70 *vs.* <30 mm	1.41 (0.91–2.18)	0.12
Missing *vs.* <30 mm	1.26 (0.83–1.90)	0.27
Neurosurgical resection within 1 year of diagnosis (yes *vs.* no)	0.76 (0.56–1.02)	0.06

HR, hazard ratio; CI, confidence interval; ICI, immune checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer.

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