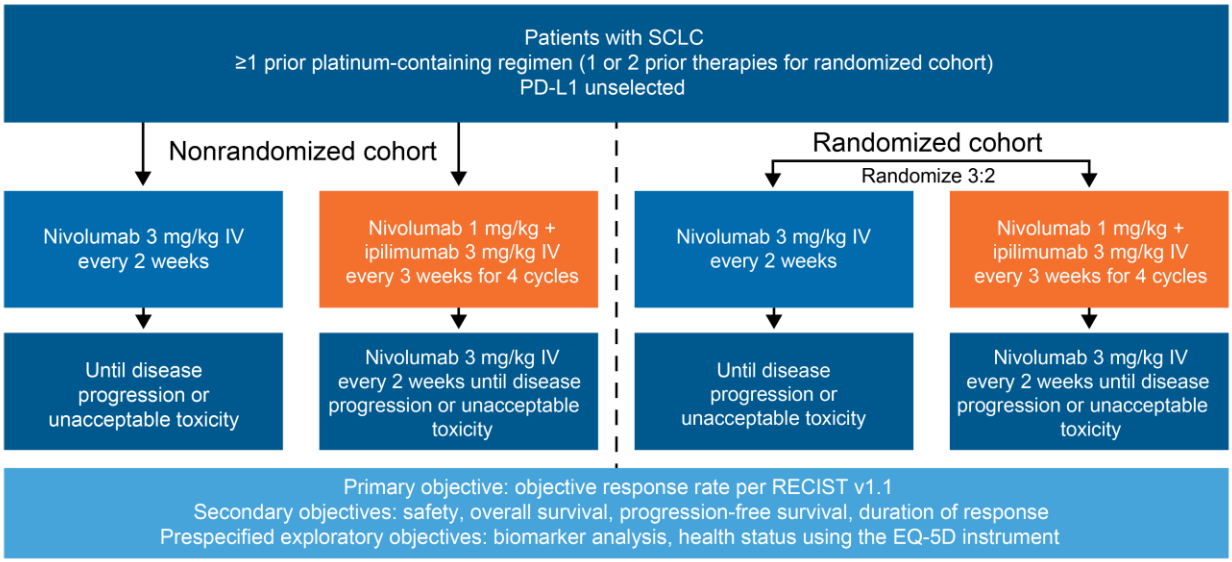


Figure S1 (Related to Figure 1). Study Design.
EQ-5D denotes EuroQoL five dimensions, IV intravenous, PD-L1 programmed death ligand 1, RECIST Response Evaluation Criteria In Solid Tumors, and SCLC small cell lung cancer.

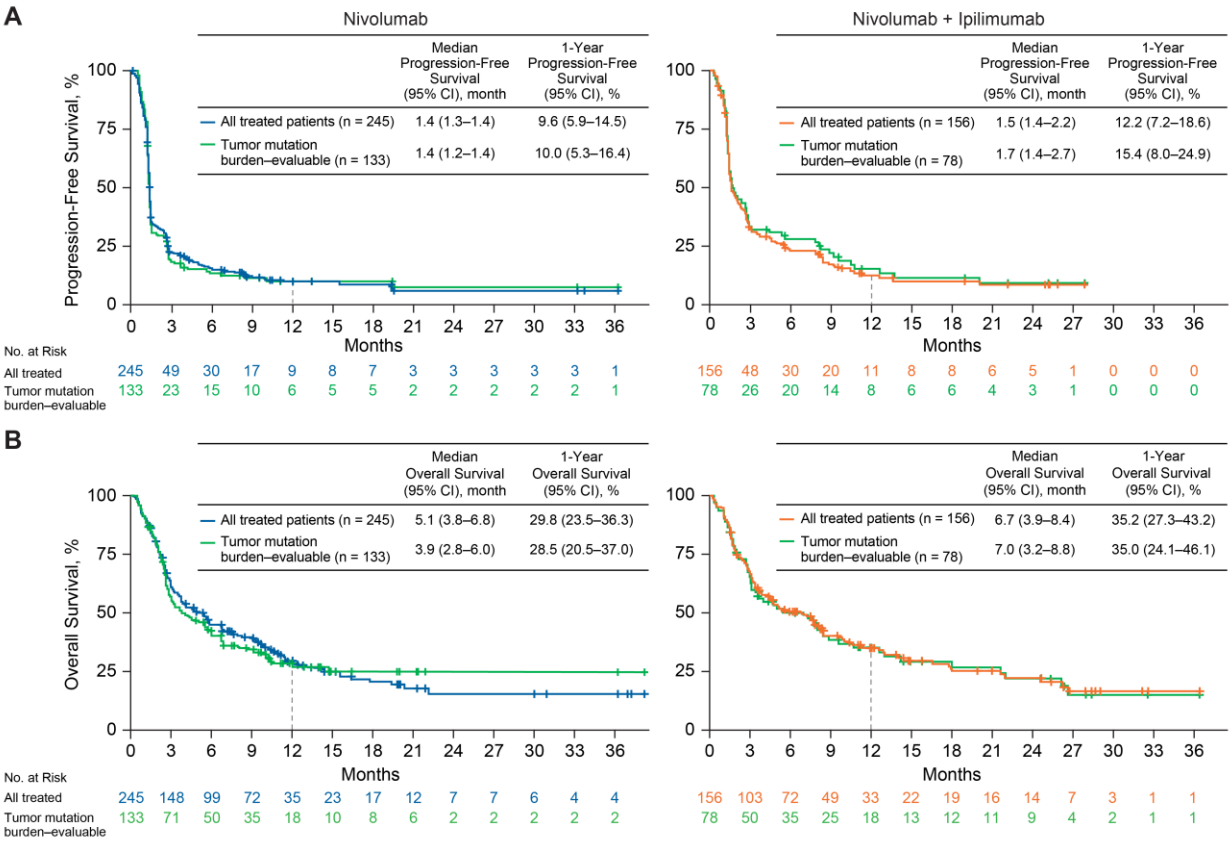
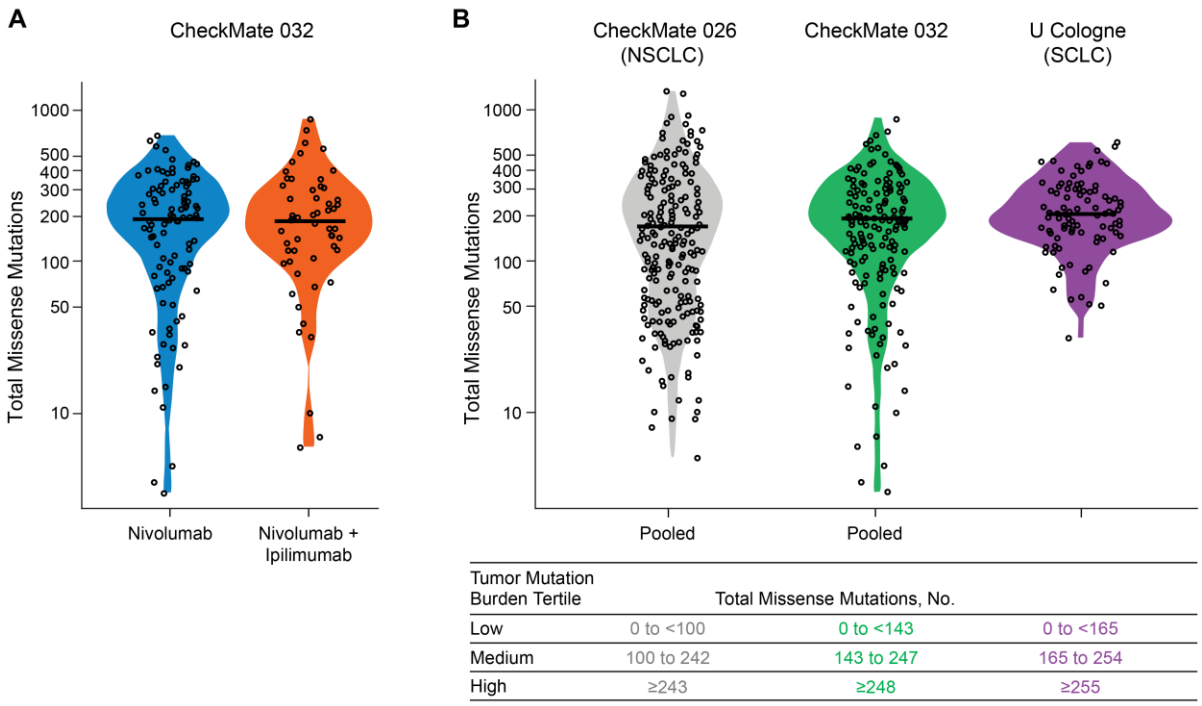


Figure S2 (Related to Figure 1). Efficacy in All Treated and Tumor Mutation Burden–Evaluable Patients by Treatment Group.

(A) Kaplan-Meier analysis of progression-free survival for nivolumab and nivolumab plus ipilimumab. (B) Kaplan-Meier analysis of overall survival for nivolumab and nivolumab plus ipilimumab. CI denotes confidence interval.



Tumor Mutation Burden Tertile	Total Missense Mutations, No.		
Low	0 to <100	0 to <143	0 to <165
Medium	100 to 242	143 to 247	165 to 254
High	≥243	≥248	≥255

Figure S3 (Related to Figure 1). Distribution of Tumor Mutation Burden.
(A) Violin plot of distribution of total missense mutations of individual patients in CheckMate 032 by treatment group. (B) Violin plot of distribution of total missense mutations of individual patients with NSCLC in CheckMate 026, SCLC in CheckMate 032, and an unrelated cohort with SCLC from the University of Cologne, regardless of treatment group. Black lines in each plot denote the median.

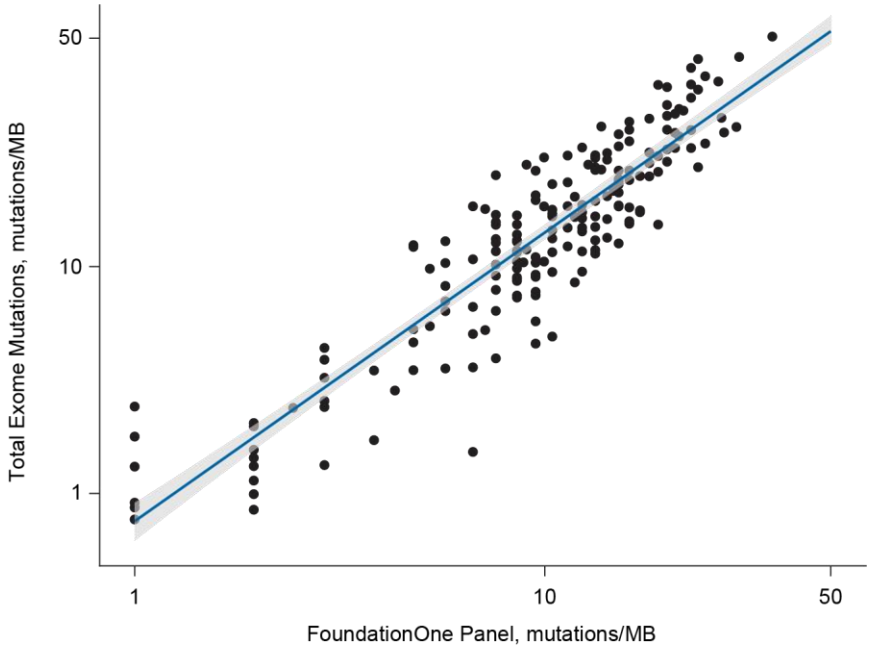


Figure S4 (Related to Figure 1). Total Exome Mutations Versus Genes in FoundationOne.
Based on in silico analysis filtering on 315 genes in FoundationOne comprehensive genomic profile (Frampton et al., 2013).

Table S1 (Related to Figure 1). Objective Response Rate in All Treated and Tumor Mutation Burden–Evaluable Patients

	Nivolumab		Nivolumab Plus Ipilimumab	
Objective Response[a]	All Treated Patients (n = 245)	TMB-Evaluable Patients (n = 133)	All Treated Patients (n = 156)	TMB-Evaluable Patients (n = 78)
No. of patients	28	15	34	22
Percent of patients (95% CI)	11.4 (7.7–16.1)	11.3 (6.5–17.9)	21.8 (15.6–29.1)	28.2 (18.6–39.5)

[a]Objective response was assessed by the investigator according to the Response Evaluation Criteria In Solid Tumors, version 1.1. The 95% confidence interval (CI) is based on the Clopper–Pearson method.

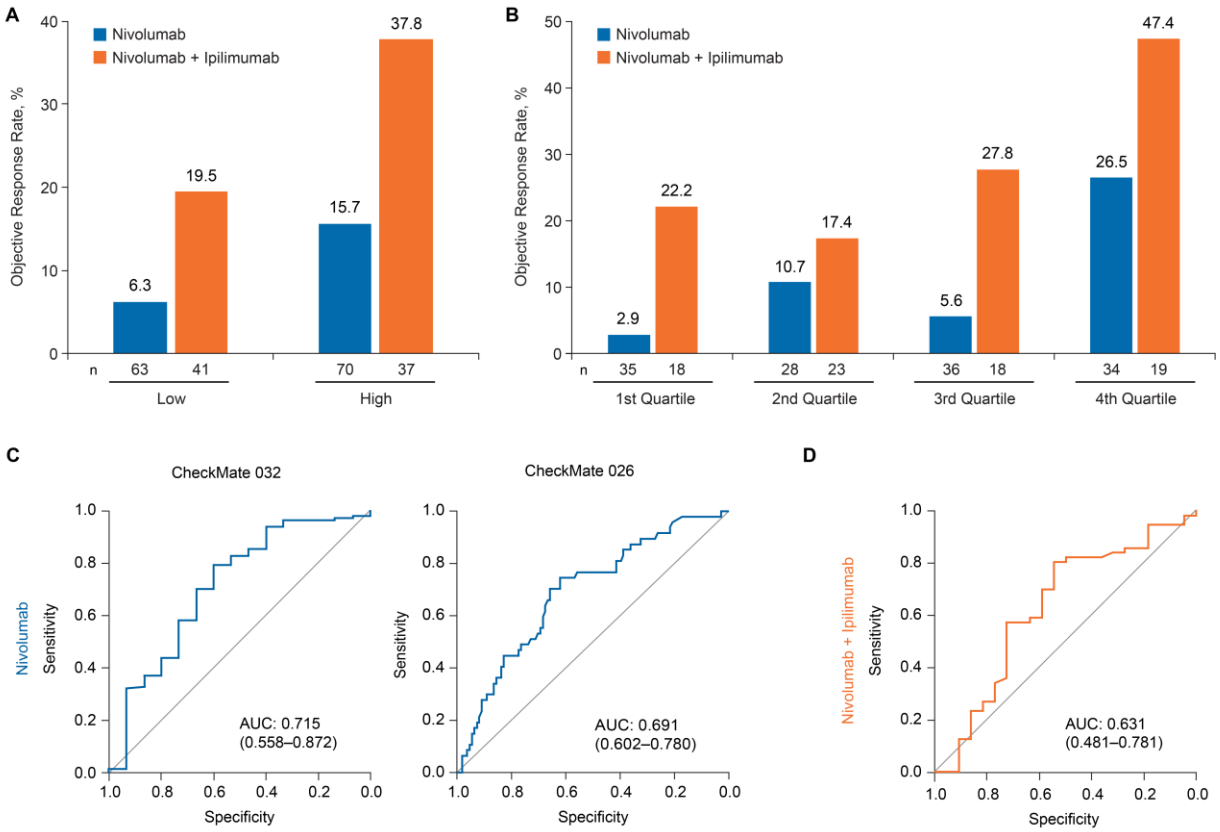


Figure S5 (Related to Figure 2). Analysis of Tumor Mutation Burden by Other Cutpoints.
(A) Objective response rate by tumor mutation burden above or below the median. (B) Objective response rate by tumor mutation burden quartile. (C) ROC analysis of tumor mutation burden and objective response rate with nivolumab monotherapy in CheckMate 032 and CheckMate 026. (D) ROC analysis of tumor mutation burden and objective response rate with nivolumab plus ipilimumab in CheckMate 032. Objective response rate was defined as the percentage of patients with complete or partial response. AUC denotes area under the curve, and ROC receiver operating characteristics.

Table S2 (Related to Figure 2). Distribution of PD-L1 Expression Among Tumor Mutation Burden–Evaluable Patients by Tertile

PD-L1 Expression — no. (%)	High TMB (n = 73)	Medium TMB (n = 69)	Low TMB (n = 69)
≥1% PD-L1	7 (9.6)	16 (23.2)	2 (2.9)
<1% PD-L1	55 (75.3)	41 (59.4)	44 (63.8)
Not evaluable	11 (15.1)	12 (17.4)	23 (33.3)

Table S3 (Related to Figure 2). Objective Response Rate by PD-L1 Status Among Patients in the Nonrandomized[a] Cohort, Regardless of Tumor Mutation Burden

	Nivolumab		Nivolumab Plus Ipilimumab	
Objective Response	≥1% PD-L1 (n = 11)	<1% PD-L1 (n = 64)	≥1% PD-L1 (n = 10)	<1% PD-L1 (n = 31)
No. of patients	1	9	1	10
Percent of patients	9.1	14.1	10.0	32.3

[a]PD-L1 data were not available for the randomized population at the time of the database lock.

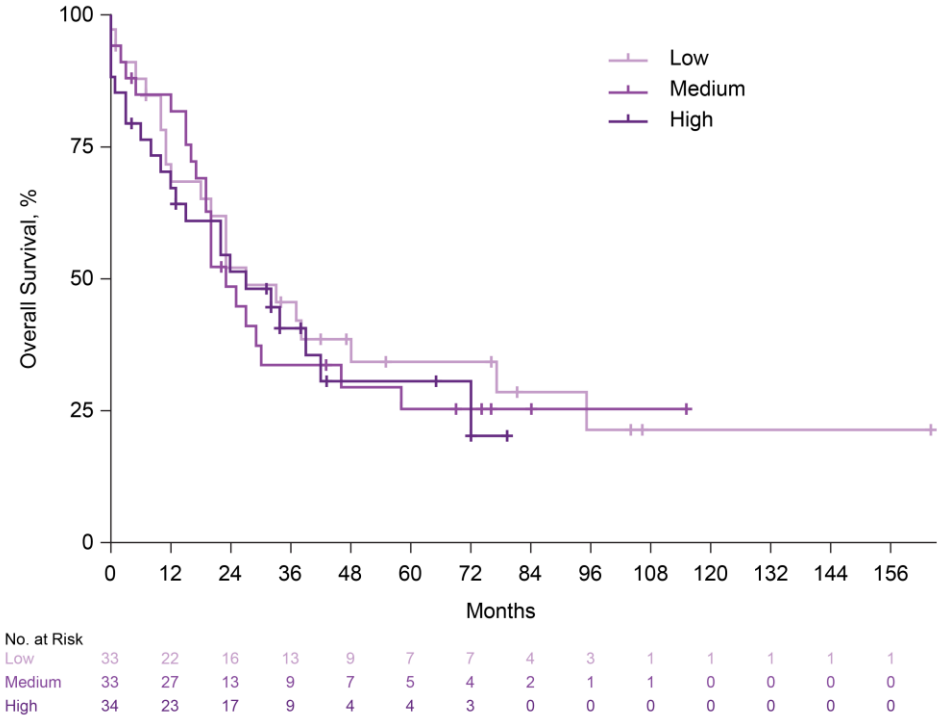


Figure S6 (Related to Figure 5). Overall Survival by Tumor Mutation Burden Tertile in an Independent Sample of Patients With SCLC.

Kaplan-Meier plot of overall survival by tumor mutation burden tertile among 100 patients in the University of Cologne data sample with available genomic and clinical data.