Background

Small cell lung cancer (SCLC) is accounted to cause for 20% of all lung cancer diagnoses in the United States and the United Kingdom.9

In clinical trials, the primary endpoint for SCLC has not substantially improved over the last decades. No new drugs have been approved for the treatment of SCLC in the past 20 years.6

• Both univariable and multivariable models (adjusted for the same factors as in the landmark analysis) were

Extended Cox model with time-varying covariate

• Within the disease is highly sensitive to first-line chemotherapy and radiotherapy, > 80% of patients experience disease progression.10 Estimated median overall survival (OS) of patients with relapsed SCLC is 6 months.1

Non-randomized comparisons between nivolumab and nivolumab + ipilimumab have been mainly reported by the CheckMate 032 study.11

Survival extrapolations in cost-effectiveness analyses for anti-cancer treatments has traditionally involved fitting parametric survival parameter-based Kaplan-Meier estimator

• To further provide evidence on the relationship between response and survival, an extended Cox model with response as a time-variant covariate was analyzed.

• The vast majority of patients with SCLC present with extensive stage disease (ED) SCLC as the disease has spread beyond their thorax. The 5-year survival rate for patients with ED SCLC is 105%

• Maintenance of the second-line treatment is beneficial for patients with SCLC and prompted use of ipilimumab as a second-line treatment for patients with SCLC who are not candidates for cisplatin-based chemotherapy.12

• Multivariable Cox models were adjusted for baseline age, gender, Eastern Cooperative Oncology Group (ECOG) status, platinum sensitivity, disease classification (LD/ED), lactate dehydrogenase, and interaction terms: disease classification*gender, disease classification*ECOG (ECOG) status, platinum sensitivity, disease classification (LD/ED), lactate dehydrogenase, and interaction

In the current study, the median follow-up time was 22 months (range, 0.1 to 41.9 months). The median overall survival (OS)2 in the nivolumab arm was 5.09 months (95% CI: 3.75–6.74) in the nivolumab arm and 6.67 months (95% CI: 3.91–8.41) in the nivolumab + ipilimumab arm. This is a significant improvement compared with historical controls.13

Extended Cox model with time-varying covariate

• Nivolumab is a fully human immunoglobulin G4 monoclonal antibody that binds to programmed death-1 (PD-1) thereby preventing activation of the PD-1 pathway. Thus, the activity of T cells against tumor cells is increased.

Lung cancer survival analysis—Including patients with stable disease in the responders category

• At 4 months, there were 24 and 29 responders among nivolumab and nivolumab + ipilimumab patients, respectively

• Patients treated with nivolumab who responded to treatment had a highly significant survival benefit compared with patients who did not respond. To further provide evidence on the relationship between response and survival, an extended Cox model with response as a time-variant covariate was analyzed.

Table 1. Multivariable Cox regression on overall survival—nivolumab arm

Table 2. Multivariable Cox regression on overall survival—nivolumab + ipilimumab arm

• The hazard ratio (HR) between responders and non-responders was 0.69 (95% CI: 0.53–0.93) in the nivolumab arm and 0.67 (95% CI: 0.50–0.89) in the nivolumab + ipilimumab arm.

• The multivariable HR = 0.29 (95% CI: 0.16–0.50); multivariable HR = 0.30 (95% CI: 0.17–0.54) in the nivolumab arm and 0.47 (95% CI: 0.25–0.89) in the nivolumab + ipilimumab arm.

• Four months was deemed to be an optimal time point allowing sufficient tumor response data and follow-up. When patients with stable disease were included in the responder category there were 50 and 49 responders in the nivolumab and nivolumab + ipilimumab arms, respectively.

• Classes of patients with SCLC in the clinical trial CheckMate 032 included those with extensive stage disease (ED) SCLC who have spread beyond their thorax and those with limited stage disease (LD) SCLC who have spread beyond their thorax and to sites only in the thorax.

• Maintenance of the second-line treatment is beneficial for patients with SCLC and prompted use of ipilimumab as a second-line treatment for patients with SCLC who are not candidates for cisplatin-based chemotherapy.12

Conclusions

• Four months was deemed as an optimal time point allowing sufficient tumor response data and follow-up.

• The results of the sensitivity analyses using alternative landmark points at 2 and 6 months were in line with the results of the primary analysis (Table 3). The c-index of 0.68 (95% CI: 0.61–0.72) was observed in the primary analysis.

References


5. FDA. https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm617370.htm.


7. FDA for the third-line treatment of SCLC6,7


