LBA5 Efficacy and safety of nivolumab (nivo) monotherapy versus chemotherapy (chemo) in recurrent small cell lung cancer (SCLC): Results from CheckMate 331

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Background: Despite high initial response rates, most patients (pts) with SCLC relapse soon after first-line (1L) treatment (tx), with limited tx options and a poor prognosis. Nivo is approved in the US for tx of metastatic SCLC with progression after platinum-based chemo and ≥1 other line of tx. We report results from CheckMate 331 (NCT02481830), a global, open-label, phase 3 trial of nivo vs chemo in pts with relapsed SCLC after 1L platinum-based chemo.

Methods: Pts (N = 569) with limited- or extensive-disease SCLC and recurrence/progression after 1L platinum-based chemo were randomized 1:1 to receive nivo (n = 284) or chemo (n = 285; topotecan or amrubicin where locally approved; see Table for all dosages), stratified by platinum sensitivity (90 days) and CNS metastases. Pts were treated until progression (or no longer deriving clinical benefit with nivo) or unacceptable toxicity. Primary endpoint was overall survival (OS) with nivo vs chemo. Approximately 482 events were expected, providing 90% power to detect a hazard ratio (HR) of 0.745 favoring nivo (2-sided alpha, 0.05).

Results: Minimum follow-up was 15.8 months. Baseline characteristics were balanced between arms. No statistically significant improvement in OS was seen with nivo vs chemo (HR, 0.86 [95% CI, 0.72–1.04]); however OS curves showed delayed separation after month 12. HR for OS with nivo vs chemo in pts with platinum-resistant SCLC was 0.71 (95% CI, 0.54–0.94). Other efficacy outcomes are shown in the table. All-grade (grade 3–4) tx-related adverse events (AE) occurred in 55% (14%) of nivo- and 90% (73%) of chemo-treated pts. There were 2 tx-related deaths with nivo and 3 with chemo.

Table: LBA5 Efficacy outcomes with nivolumab vs chemotherapy in recurrent SCLC

	Nivo[a] (n = 284)	Chemo[b] (n = 285)
Overall survival		
Events, n (%)	225 (79)	245 (86)
Median, months (95% CI)	7.5 (5.7–9.2)	8.4 (7.0–10.0)
HR (95% CI)	0.86 (0.72–1.04) P = 0.11[c]	
1-year OS rate, % (95% CI)	37 (31–42)	34 (29–40)
Progression-free survival		
Events, n (%)	258 (91)	235 (82)
Median, months (95% CI)	1.4 (1.4–1.5)	3.8 (3.0–4.2)
HR (95% CI)	1.41 (1.18–1.69)	
1-year PFS rate, % (95% CI)	11 (8–15)	10 (7–14)
Objective response rate, n (%)	39 (14)	47 (16)
Odds ratio (95% CI)	0.80 (0.50–1.27)	
Duration of response		
n events/n responders (%)	28/39 (72)	43/47 (92)
Median, months (95% CI)	8.3 (7.0–12.6)	4.5 (4.1–5.8)

[a]240 mg IV Q2W.
[b]Topotecan 1.5 mg/m^2 IV or 2.3 mg/m^2 oral daily on days 1–5 of a 21-day cycle or amrubicin 40 mg/m^2 IV daily on days 1–3 of a 21-day cycle.
[c]P value calculated from log-rank test stratified by response to 1L platinum-based therapy (sensitive vs refractory/resistant) and baseline CNS metastases (yes vs no) per interactive voice response system.

Conclusions: CheckMate 331 did not meet the primary endpoint of OS for nivo vs chemo in 2L SCLC. However, late separation of curves and potential activity in the platinum-refractory setting suggests possible long-term benefit for some pts. There were no new safety signals, with lower AE rates observed with nivo.

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