Check Mate-032

(PD1/PDL1-62/158)

Check Mate-032

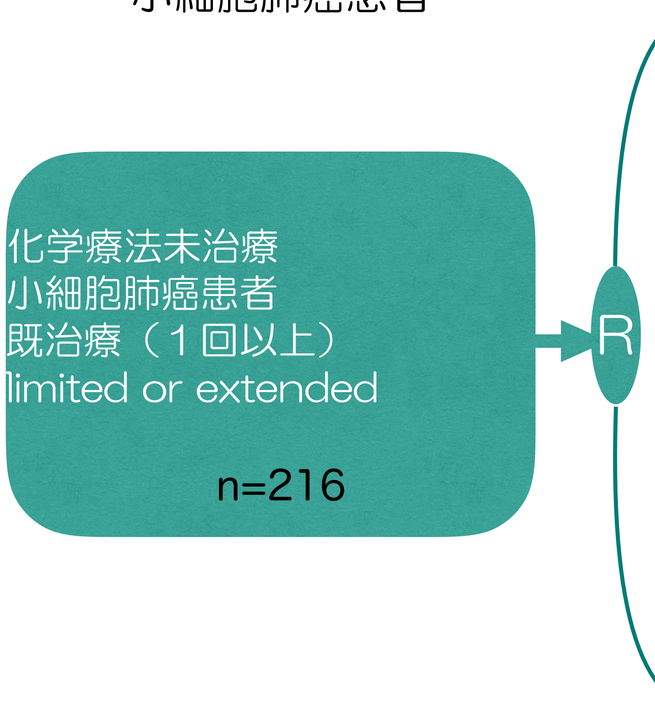
6カ国２３施設

Primary Endpoint: ORR(by investigator)

Secondary Endpoint: duration of response, PFS, OR and safety

Lancet Oncol 2016

interim analysis of the SCLC cohort

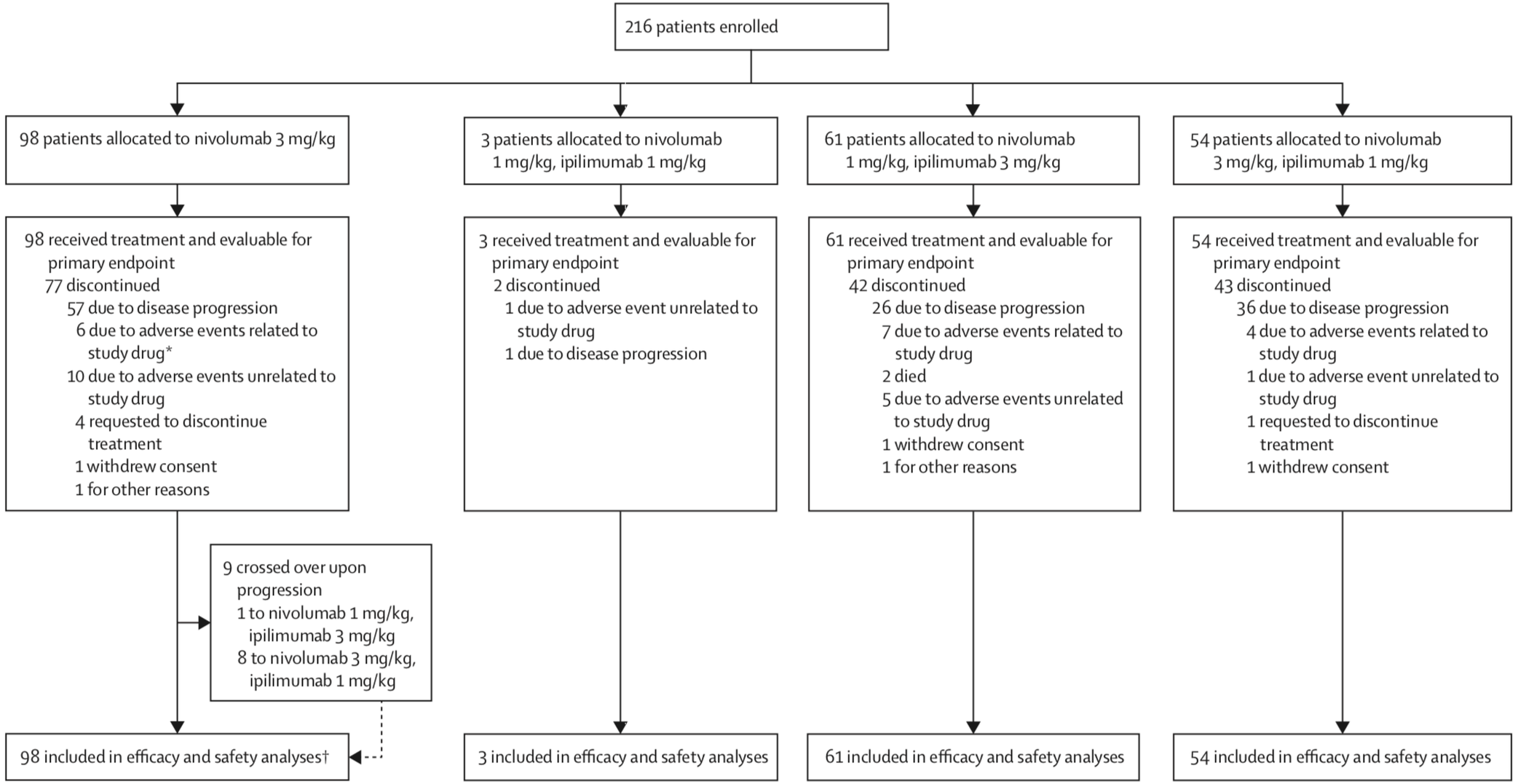


	median follow up date	ORR	Grade3/4 AE	discontinued treatment
3mg/kg, every two week Nivolumab n=98	198.5 days	10% (10/98)	13% (13/98)	6% (6/98)
1mg/kg, every two week Nivolumab + Ipilimumab n=3 1mg/kg, every two week	302 days	33% (1/3)		
1mg/kg, every two week Nivolumab + Ipilimumab n=61 3mg/kg, every two week	361 days	23% (14/61)	30% (18/61)	11% (7/61)
3mg/kg, every two week Nivolumab + Ipilimumab n= 54 1mg/kg, every two week	260.5 days	19% (10/54)	19% (10/54)	7% (4/54)

(PD1/PDL1-105)

Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate 032): a multicentre, open-label, phase 1/2 trial

interim analysis of the SCLC cohort



(PD1/PDL1-62)

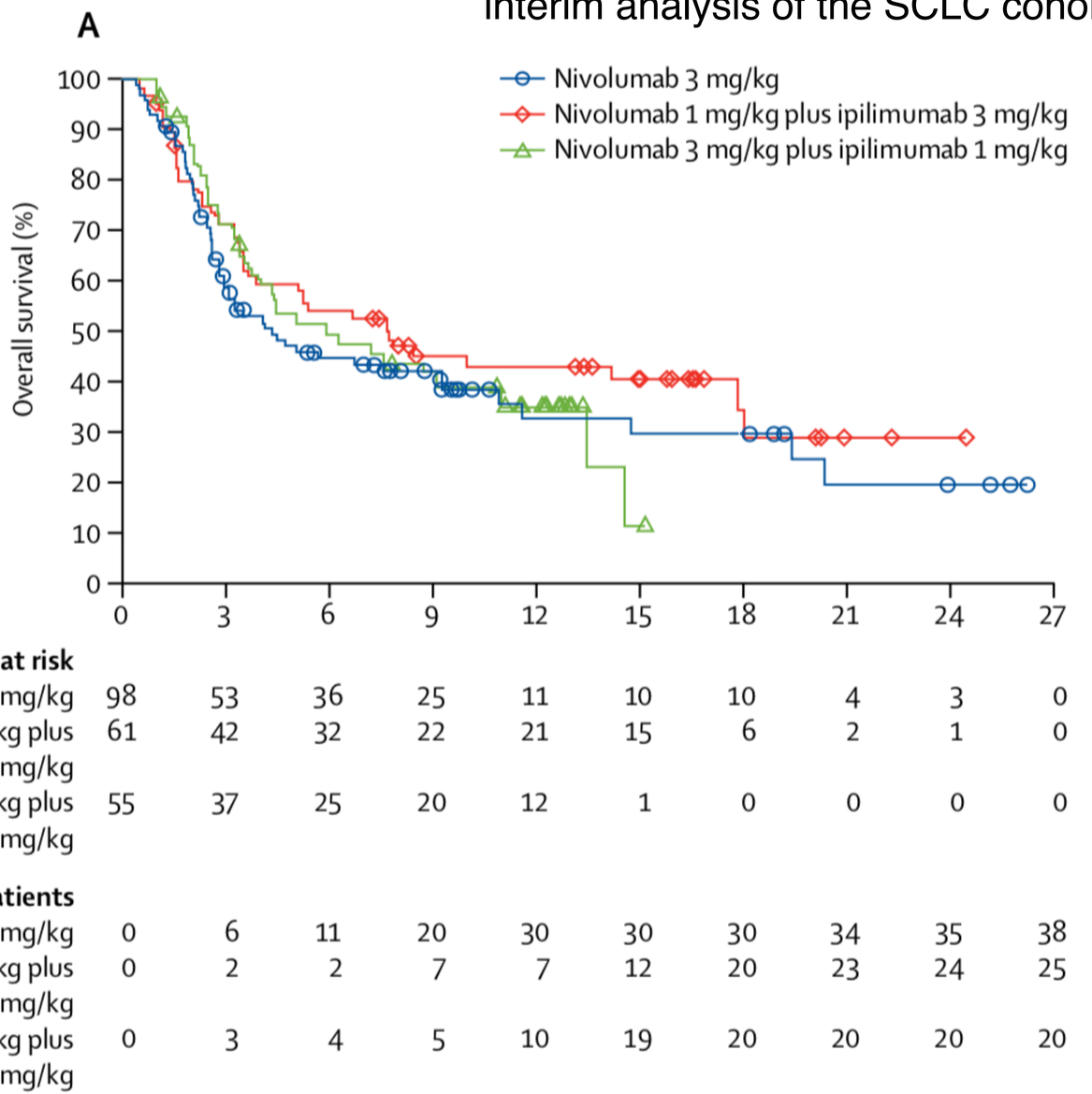
Lancet Oncol 2016

interim analysis of the SCLC cohort

	Nivolumab 3 mg/kg (n=98)	Nivolumab 1 mg/kg plus ipilimumab 3 mg/kg (n=61)	Nivolumab 3 mg/kg plus ipilimumab 1 mg/kg (n=54)
Objective response; 95% CI	10 (10%; 5–18)	14 (23%; 13–36)	10 (19%; 9–31)
Best overall response			
Complete response	0	1 (2%)	0
Partial response	10 (10%)	13 (21%)	10 (19%)
Stable disease	22 (22%)	13 (21%)	9 (17%)
Progressive disease	52 (53%)	23 (38%)	29 (54%)
Unable to determine	12 (12%)	8 (13%)	6 (11%)
Not reported	2 (2%)	3 (5%)	0
Time to objective response (IQR), months	2·0 (1·3–2·8)	2·1 (1·4–2·8)	1·4 (1·3–2·7)

Data are n (%) unless otherwise stated. All patients were enrolled at least 90 days prior to database lock.

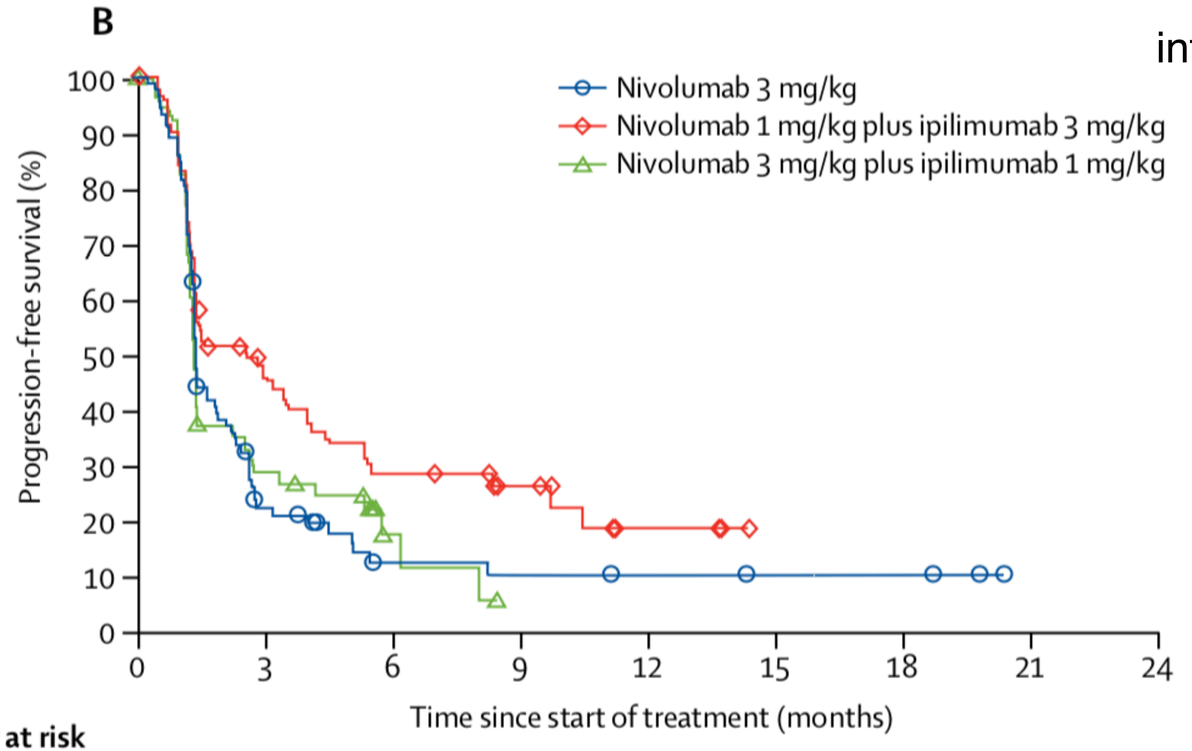
Table 2: **Tumour response**



(PD1/PDL1-62)

Lancet Oncol 2016

interim analysis of the SCLC cohort



Number at risk									
Nivolumab 3 mg/kg	98	17	6	5	4	3	3	0	0
Nivolumab 1 mg/kg plus ipilimumab 3 mg/kg	61	24	15	9	3	0	0	0	0
Nivolumab 3 mg/kg plus ipilimumab 1 mg/kg	54	14	3	0	0	0	0	0	0
Number of censored patients									
Nivolumab 3 mg/kg	0	12	17	17	18	19	19	22	22
Nivolumab 1 mg/kg plus ipilimumab 3 mg/kg	0	5	5	10	14	17	17	17	17
Nivolumab 3 mg/kg plus ipilimumab 1 mg/kg	0	4	11	12	12	12	12	12	12

(PD1/PDL1-62)

Check Mate-032

Primary Endpoint: ORR (by BICR)

Secondary Endpoint: duration of response, PFS, OR and safety

third- or later-line nivolumab monotherapy treatment

JTO 2019

6カ国２３施設

An international real-world, retrospective analysis evaluating third-line chemotherapy treatment in patients with SCLC (N=120) reported a median OS time of 4.7 months and response rate of 18%; of note, DOR was not reported in this study.[17]

小細胞肺癌患者

化学療法未治療
小細胞肺癌患者
既治療（１回以上）
limited or extended

n=216

n=109

Nivolumab
3mg/kg, every two week

third- or later-line nivolumab monotherapy treatment

median follow up date	ORR	median duration of response	6ヶ月 PFS	OR 12ヶ月	OR 18ヶ月	Grade3/4 AE	discontinued treatment
28.3ヶ月	11.9%	17.9ヶ月	17.2%	28.3ヶ月	20.0ヶ月	11.9%	2.8%

The median duration of response (DOR) with intravenous topotecan is 3.3 months,

No selection by biomarker such as tumor PD-L1 expression

On August 16, 2018, on the basis of the results presented in this article, nivolumab monotherapy received approval by the U.S. Food and Drug Administration (FDA) for the treatment of patients with metastatic SCLC with progression after platinum-based chemotherapy and at least one other line of therapy.

(PD1/PDL1-105)

Journal of Thoracic Oncology Vol. 14 No. 2: 237-244

We report results of third- or later-line nivolumab monotherapy treatment in SCLC.

Third-Line Nivolumab Monotherapy in Recurrent SCLC: CheckMate 032

The median duration of response (DOR) with intravenous topotecan is 3.3 months,

Table 1. Baseline Characteristics of Patients Treated with Third-or Later-Line Nivolumab Monotherapy

Characteristic	Third- or Later-Line Nivolumab (n = 109)
Median age, y (range)	64.0 (45-81)
≥75 y, n (%)	7 (6.4)
Male, n (%)	61 (56.0)
Race, n (%)	
White	102 (93.6)
Black/African American	4 (3.7)
Other	3 (2.8)
Prior systemic treatment regimens, n (%)	
2	78 (71.6)
3	25 (22.9)
>3	6 (5.5)
First-line platinum-treated patients, n (%)	
Platinum-sensitive[a]	71 (65.1)
Platinum-resistant[b]	37 (33.9)
Unknown	1 (0.9)
Smoking status, n (%)	
Current/former smoker	101 (92.7)
Never smoker	8 (7.3)
ECOG PS, n (%)	
0	32 (29.4)
1	76 (69.7)
2[c]	1 (0.9)
Tumor PD-L1 expression, n (%)	
<1%	65 (59.6)
≥1%	13 (11.9)
Not quantifiable[d]	31 (28.4)

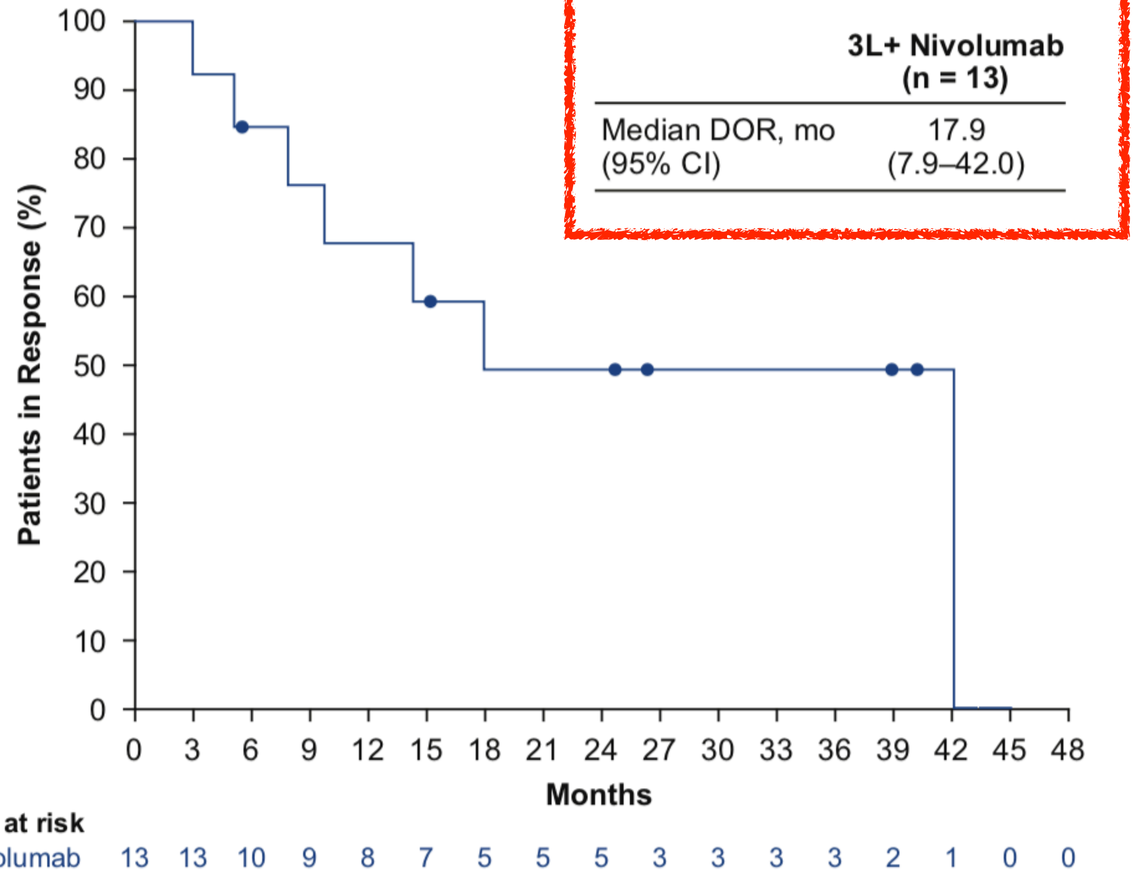


Figure 1. Duration of response (DOR) by blinded independent central review with third- or later-line (3L+) nivolumab monotherapy. CI, confidence interval.

(PD1/PDL1-158)

Journal of Thoracic Oncology Vol. 14 No. 2: 237-244

We report results of third- or later-line nivolumab monotherapy treatment in SCLC.

Table 2. ORRs with Third-or Later-Line Nivolumab Monotherapy

Endpoint	Third-or Later-Line Nivolumab (n = 109)
ORR by BICR[a]	
No. of patients	13
% of patients (95% CI)	11.9 (6.5-19.5)
Best overall response, n (%)	
Complete response	1 (0.9)
Partial response	12 (11.0)
Stable disease	25 (22.9)
Progressive disease	56 (51.4)
Unable to determine	14 (12.8)
Not reported	1 (0.9)
Median time to response, mo	1.6
Duration of response	
≥6 mo, n (%)	10 (76.9)
≥12 mo, n (%)	8 (61.5)
Median (95% CI), mo[b]	17.9 (7.9-42.0)
Range, mo	3.0-42.1

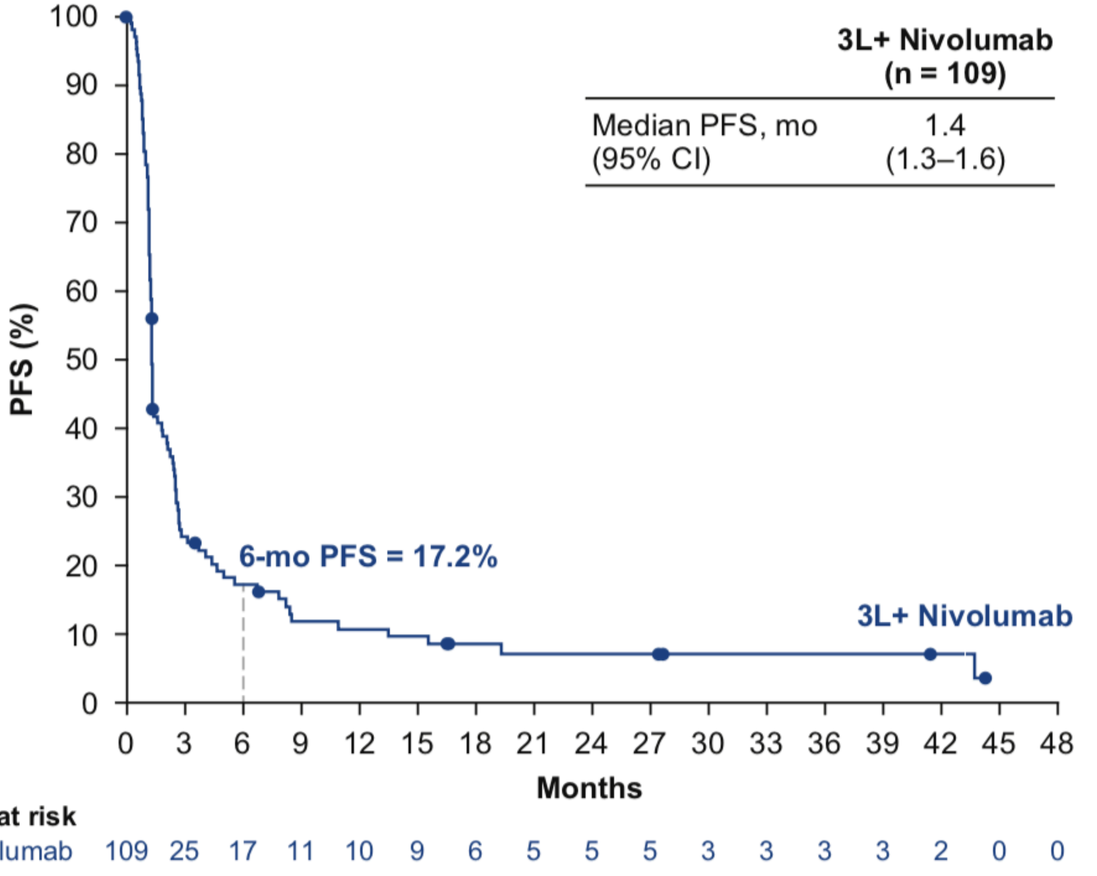


Figure 2. Progression-free survival (PFS) by blinded independent central review with third- or later-line (3L+) nivolumab monotherapy. CI, confidence interval.

(PD1/PDL1-158)

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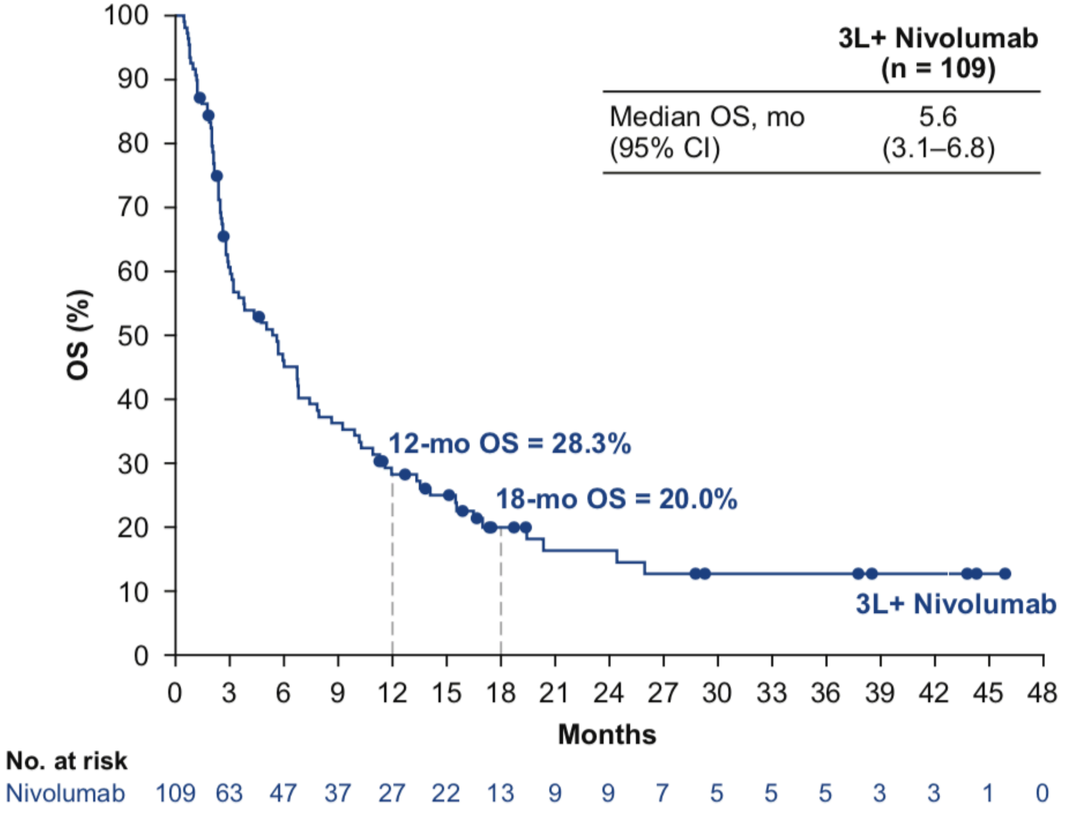

Figure 3. Overall survival (OS) with third- or later-line (3L+) nivolumab monotherapy. CI, confidence interval.

Table 3. Treatment-Related Adverse Events

Event, n (%)	Third-or Later-Line Nivolumab (n = 109) Any Grade	Grade 3-4
Any event	60 (55.0)	13 (11.9)
Any serious event	9 (8.3)	8 (7.3)
Any event leading to discontinuation	3 (2.8)	3 (2.8)
Most frequent events (≥5%)		
Pruritus	14 (12.8)	0
Fatigue	11 (10.1)	1 (0.9)
Nausea	8 (7.3)	0
Rash	7 (6.4)	1 (0.9)
Diarrhea	7 (6.4)	0
Decreased appetite	6 (5.5)	1 (0.9)

(PD1/PDL1-158)