Assessment of hyperprogression versus the natural course of disease development with nivolumab with or without ipilimumab versus placebo in phase III, randomized, controlled trials

Online Supplemental Tables and Figures

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Online Supplemental Table S1. Patient demographics and baseline characteristics for patients excluded from the ATTRACTION-2 HPD analysis population

Characteristic	Placebo (n = 48)	Nivolumab 3 mg/kg (n = 87)
Age, years, median (range)	60 (28–79)	56 (24–79)
Female, n (%)	16 (33)	41 (47)
Race, n (%)		
Asian	48 (100)	87 (100)
Native Hawaiian/other Pacific Islander	0	0
ECOG PS, n (%)		
0	10 (21)	21 (24)
1	38 (79)	66 (76)
Baseline tumor size, cm		
n	16	25
Mean (SD)	6.93 (5.39)	8.12 (4.94)
Median (range)	4 (1.2–17.9)	9.5 (1.4–16.2)

ECOG PS, Eastern Cooperative Oncology Group performance status;
HPD, hyperprogressive disease; SD, standard deviation.

Online Supplemental Table S2. Demographics and baseline characteristics of nivolumab-treated patients with target lesion SLD increases ≥200% in the ATTRACTION-2 study.

Characteristic	Patient 1	Patient 2	Patient 3
Age, years	67	55	59
Sex	F	M	M
ECOG PS	1	1	1
Disease stage	IIIC	IV	IIIC
Macroscopic tumor type (Borrman's classification)	Advanced carcinoma type II	Unknown	Advanced carcinoma type I
Histological type (Lauren classification)	Other	Unknown	Unknown
Number of organs with metastases	1	3	1
Smoking status	Never	Never	Former
Alcohol consumption status	Never	Never	Former
Baseline target lesion SLD, cm	2.2	5.4	2.2

ECOG PS, Eastern Cooperative Oncology Group performance status; F, female; M, male; SLD, sum of the longest diameters.

Online Supplemental Table S3. *MDM2* CNAs and % TGR at the first on-treatment scan in 4 of 91 patients with genomic data in the ATTRACTION-2 nivolumab 3 mg/kg study arm

Patient identifier*	*MDM2* CNA	% TGR at the first scan	BOR	OS, months/censoring
1	Amplification (8, exons 11 of 11)	−16.2	PR	8.9; 1
2	Amplification (15, exons 11 of 11)	−3.4	SD	14.0; 1
3	Amplification (13, exons 11 of 11)	58.1	PD	3.5; 0
4	Amplification (61, exons 11 of 11)	Not available	NE	1.2; 0

BOR, best overall response; CNA, copy number alteration; NE, not evaluable; OS, overall survival; PD, progressive disease; PR, partial response; SD, stable disease; TGR, tumor growth rate.
*Arbitrary patient identifier numbers.

Online Supplemental Table S4. EGFR alterations and % TGR at the first on-treatment scan in 6 of 91 patients with genomic data in the ATTRACTION-2 nivolumab 3 mg/kg study arm

Patient identifier*	*EGFR* alteration	% TGR at the first scan	BOR	OS, months/censoring
1	Amplification (8, exons 30 of 30)	−31	PR	12.5; 1
2	Amplification (81, exons 30 of 30), *EGFR* rearrangement	3	SD	8.3; 0
3	Amplification (7, exons 30 of 30)	5	PD	2.5; 0
4	Amplification (125, exons 30 of 30), *EGFR* rearrangement	24	PD	3.7; 0
5	Amplification (9, exons 28 of 30), *EGFR* rearrangement	29	PD	2.4; 0
6	Amplification (122, exons 30 of 30)	92	NE	0.9; 0

BOR, best overall response; NE, not evaluable; OS, overall survival; PD, progressive disease; PR, partial response; SD, stable disease; TGR, tumor growth rate.
*Arbitrary patient identifier numbers.

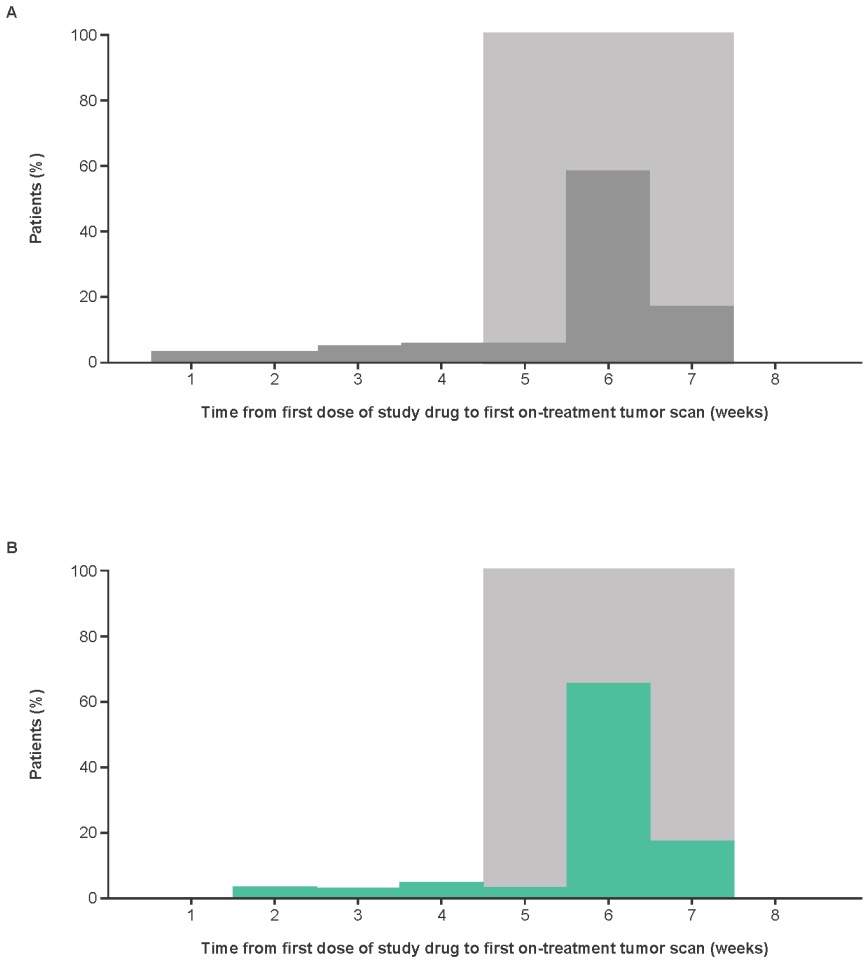
Online Supplemental Table S5. Patient demographics and baseline characteristics for patients excluded from the CheckMate 451 HPD analysis population

Characteristic	Placebo (n = 100)	Nivolumab 240 mg (n = 103)	Nivolumab 1 mg/kg + ipilimumab 3 mg/kg (n = 100)
Age, years, median (range)	63 (44–84)	65 (32–84)	65 (47–80)
Female, n (%)	40 (40)	41 (40)	39 (39)
Race, n (%)			
White	71 (71)	75 (73)	75 (75)
Black or African American	1 (1)	4 (4)	0
Asian	27 (27)	23 (22)	24 (24)
Other	1 (1)	1 (1)	
Not reported	0	0	1 (1)
ECOG PS, n (%)			
0	42 (42)	41 (40)	33 (33)
1	58 (58)	62 (60)	67 (67)
Region, n (%)			
US/Canada	22 (22)	21 (20)	26 (26)
Asia	27 (27)	21 (20)	24 (24)
Europe	35 (35)	42 (41)	39 (39)
Rest of world	16 (16)	19 (18)	11 (11)
Type of first-line, platinum-based therapy, n (%)*			
Carboplatin	57 (57)	66 (64)	68 (68)
Cisplatin	46 (46)	43 (42)	34 (34)
Baseline tumor size, cm			
n	18	19	21
Mean (SD)	7.10 (5.69)	6.66 (4.86)	5.42 (4.34)
Median (minimum, maximum)	4.8 (1.5–19.4)	4.8 (1.1–18.1)	3.9 (1.4–20.4)

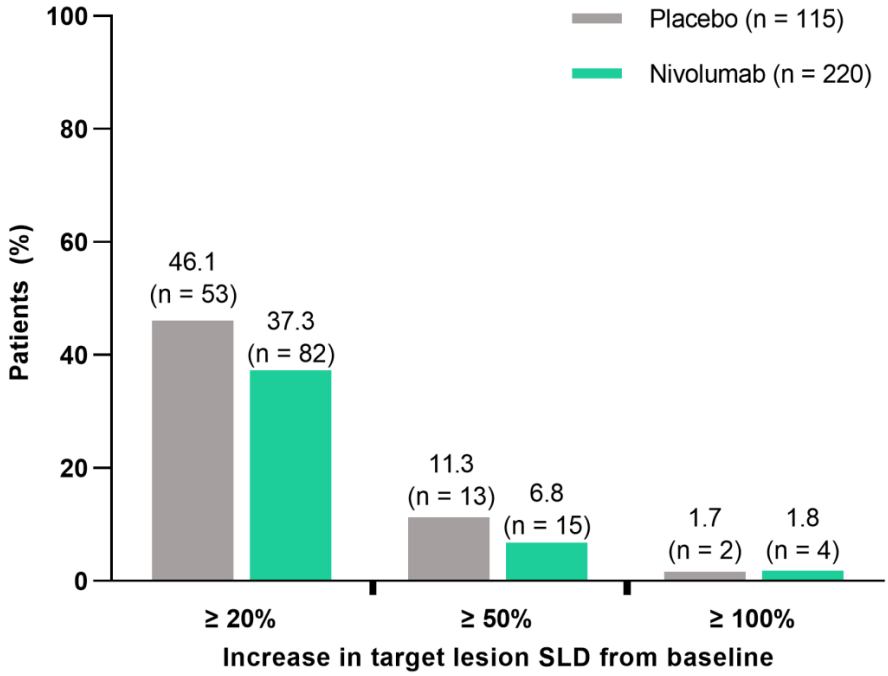
ECOG PS, Eastern Cooperative Oncology Group performance status; HPD, hyperprogressive disease; SD, standard deviation.

*Patients may have received more than one type of platinum compound.

Online Supplemental Figure S1. Distribution of timing of first post-treatment scan in patients randomized to (A) placebo and (B) nivolumab 240 mg Q2W in the ATTRACTION-2 study. The light gray shaded area indicates the protocol-defined window for first post-treatment scan at week 6 (range, 5–7 weeks). Q2W, every 2 weeks.

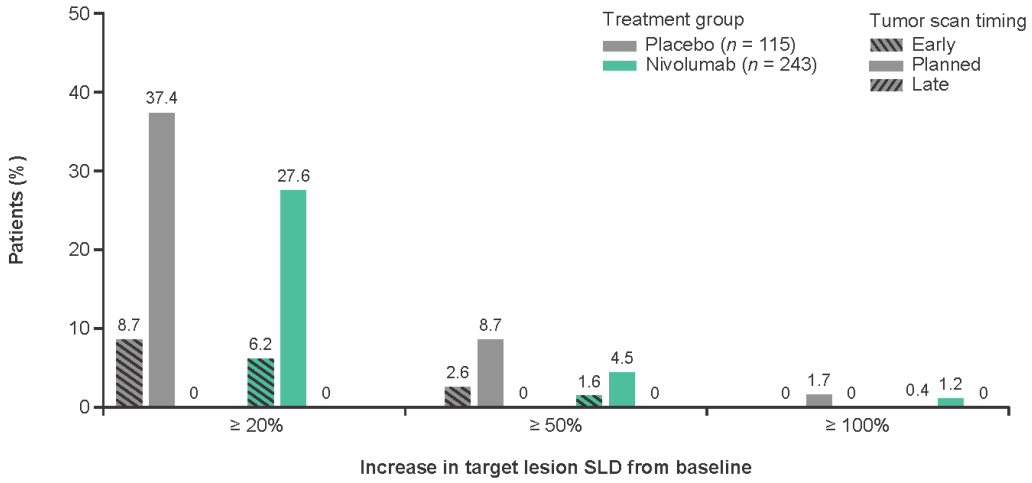


Online Supplemental Figure S2. Proportions of patients with ≥20%, ≥50%, and ≥100% increases from baseline in target lesion SLD at the first on-treatment scan in patients with a best response of SD or PD at the first assessment in ATTRACTION-2.

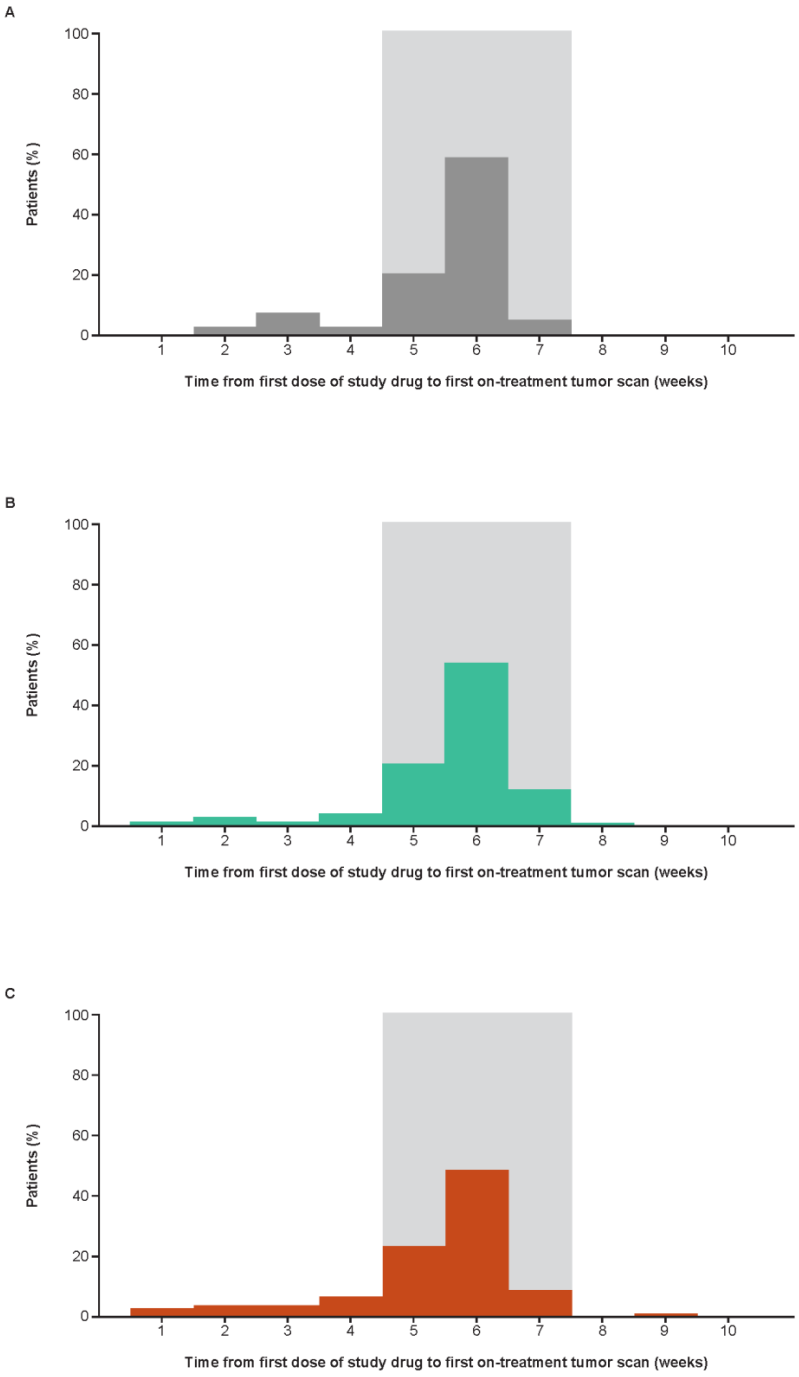


PD, progressive disease; SD, stable disease; SLD, sum of the longest diameters.

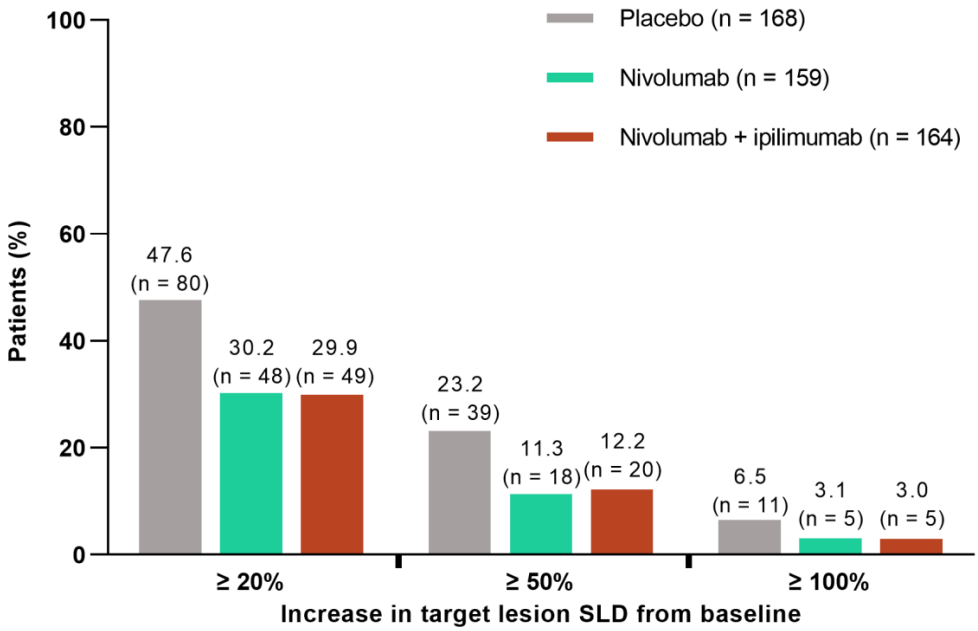
Online Supplemental Figure S3. Proportions of patients with ≥20%, ≥50%, and ≥100% increases from baseline in target lesion SLD at the first on-treatment scan in ATTRACTION-2 by timing of first on-treatment scan relative to the start of treatment. SLD, sum of the longest diameters.



Online Supplemental Figure S4. Distribution of timing of first post-treatment scan in patients randomized to (A) placebo, (B) nivolumab 240 mg Q2W, and (C) nivolumab 1 mg/kg plus ipilimumab 3 mg/kg Q2W in CheckMate 451. The light gray shaded area indicates the protocol-defined window for the first post-treatment scan at week 6 (range, 5–7 weeks). Q2W, every 2 weeks.



Online Supplemental Figure S5. Proportions of patients with ≥20%, ≥50%, and ≥100% increases from baseline in target lesion SLD at the first on-treatment scan in patients with a best response of SD or PD at the first assessment in CheckMate 451.



PD, progressive disease; SD, stable disease; SLD, sum of the longest diameters.

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Online Supplemental Figure S6. Proportions of patients with ≥20%, ≥50%, and ≥100% increases from baseline in target lesion SLD at the first on-treatment scan in CheckMate 451 by timing of first on-treatment scan relative to the start of treatment. SLD, sum of the longest diameters.