Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Next-Line Therapies

Agents	Regimen	ECOG PS 0-1 (N = 31)	ECOG PS ≥2 (N = 24)
Pembrolizumab + Chemotherapy	Pembrolizumab + Carboplatin + Pemetrexed	3	
	Pembrolizumab + Carboplatin + Paclitaxel	1	
	Pembrolizumab + Pemetrexed	1	
Chemotherapy	Carboplatin + Pemetrexed	2	
	Carboplatin + Paclitaxel	1	
	Carboplatin + Gemcitabine	1	
	Docetaxel	2	
Targeted therapy	Osimertinib	1	1
	Alectinib	1	
	Dabrafenib + Trametinib		1
Clinical Trials		1	
Total		**14**	**2**

eTable 2. Unadjusted Association Between Baseline Clinicopathologic/Laboratory Characteristics and Patient Outcomes

	Unadjusted HR for progression or death (95% CI)	**P value**	**Unadjusted HR for death (95% CI)**	**P value**
ECOG PS (2-3 versus 0-1)	**2.24 (1.28 – 3.92)**	**0.005**	**3.59 (1.94 – 6.65)**	**<0.001**
Age (years	1.01 (0.98 – 1.04)	0.42	1.03 (0.99 – 1.06)	0.09
Sex (Female versus Male)	1.65 (0.94 – 2.89)	0.08	1.39 (0.78 – 2.49)	0.27
Race (Caucasian versus Non-Caucasian)	0.79 (0.42 – 1.54)	0.50	0.63 (0.31 – 1.27)	0.19
Body mass index	1.01 (0.97 – 1.05)	0.66	1.00 (0.95 – 1.05)	0.96
Obese (Yes versus No)	1.36 (0.69 – 2.65)	0.38	1.44 (0.69 – 3.02)	0.33
Ever smoker, (No versus Yes)	2.84 (0.99 – 8.20)	0.05	1.76 (0.74 – 4.19)	0.20
Simplified Comorbidity score	0.98 (0.89 – 1.08)	0.67	1.03 (0.94 – 1.14)	0.48
Hypertension (Yes versus No)	1.08 (0.62 – 1.88)	0.79	1.35 (0.75 – 2.43)	0.32
Diabetes mellitus (Yes versus No)	1.24 (0.52 – 2.94)	0.62	1.69 (0.78 – 3.68)	0.18
Cardiovascular Comorbidities (Yes versus No)	0.93 (0.53 – 1.63)	0.80	1.25 (0.69 – 2.27)	0.46
Respiratory Comorbidities (Yes versus No)	0.89 (0.49 – 1.59)	0.69	1.10 (0.58 – 2.09)	0.76
Creatinine clearance <60 (Yes versus No)	1.04 (0.58 – 1.85)	0.90	1.36 (0.74 – 2.47)	0.32
Creatinine clearance <30 (Yes versus No)	1.52 (0.47 – 4.94)	0.48	2.64 (0.81 – 8.61)	0.11
VTE (Yes versus No)	0.85 (0.41 – 1.76)	0.67	0.87 (0.39 – 1.91)	0.73
PD-L1 TPS (%)	0.99 (0.99 – 1.01)	0.77	0.99 (0.99 – 1.01)	0.51
Number of metastatic sites	1.14 (0.93 – 1.39)	0.19	1.12 (0.90 – 1.38)	0.31
Lung/pleura metastases (Yes versus No)	0.79 (0.45 – 1.39)	0.42	0.72 (0.39 – 1.30)	0.27
Lymph node metastases (Yes versus No)	1.25 (0.71 – 2.17)	0.44	1.09 (0.59 – 1.99)	0.78
Brain metastases (Yes versus No)	1.05 (0.58 – 1.89)	0.87	1.15 (0.61 – 2.15)	0.67
Bone metastases (Yes versus No)	1.61 (0.92 – 2.83)	0.09	1.41 (0.78 – 2.56)	0.26
Liver metastases (Yes versus No)	1.81 (0.76 – 4.32)	0.18	1.54 (0.68 – 3.49)	0.29

Adrenal metastases (Yes versus No)	1.26 (0.54 – 2.98)	0.59	1.67 (0.70 – 3.97)	0.25
Other metastases (Yes versus No)	1.39 (0.65 – 2.97)	0.39	1.44 (0.71 – 2.91)	0.32
Line of therapy (≥ Second line versus First line)	1.02 (0.55 – 1.89)	0.95	0.97 (0.49 – 1.88)	0.92
White blood cell count (K/uL)	**1.06 (1.01 – 1.12)**	**0.01**	**1.08 (1.03 – 1.13)**	**0.003**
Absolute neutrophil count (K/uL)	**1.07 (1.01 – 1.14)**	**0.02**	**1.09 (1.03 – 1.17)**	**0.004**
Creatinine (mg/dL)	0.94 (0.53 – 1.68)	0.84	1.22 (0.68 – 2.18)	0.66

Abbreviations: CAD = Coronary artery disease, CHF = Congestive heart failure, CI = Confidence intervals, ECOG PS = Eastern Cooperative Oncology group performance status, HR = Hazard ratio, K/uL = x1000/microliter, NSCLC = Non-small-cell lung cancer, PD-L1 = Programmed death ligand -1, TPS = Tumor proportion score, VTE = Venous thromboembolic disease

eTable 3. Comparison of Efficacy and Survival Outcomes Reported in Literature on Treatment With Immune Checkpoint Inhibitors in Patients With Advanced NSCLC with ECOG PS of at Least 2

	Retrospective					Prospective Non-randomized
	Sehgal *et al*	**Petrillo *et al***	**Facchinetti *et al***	**Alessi *et al***	**Friedlaender *et al***	**Middleton *et al***
ICI	Pembrolizumab	Nivolumab, Pembrolizumab, Atezolizumab	Pembrolizumab	Pembrolizumab	Pembrolizumab	Pembrolizumab
PS	2 - 3	2 - 4	2	2	2	2
PD-L1	**Any**	**Any**				**Any**
Line	**Any**	**Any**				**Any**
N	29	84				60
ORR, %	17.9 %	Not reported				27 %
DCR, %	53.6 %	Not reported				37 %
Median PFS, mo (95% CI)	2.3 (1.8 – 4.8)	1.7 (1.3 – 2.1)				4.4 (3.3 – 9.9)
Median OS, mo (95% CI)	4.1 (2.1 – 6.9)	4.5 (2.3 – 6.9)				9.8 (7.1 – 14.6)
PD-L1	**Any**	**Any**				**Any**
Line	**First**	**First**				**First**
N	21	19				24
ORR, %	20 %	Not reported				21 %
DCR, %	55 %	Not reported				38 %
Median PFS, mo (95% CI)	2.7 (1.8 – 7.6)	Not reported				4.3 (1.9 – 13.1)
Median OS, mo (95% CI)	4.3 (2.3 – 7.8)	6.7 (Not reported)				7.9 (2.6 – Not reached)
PD-L1	**≥ 50%**					**≥ 50%**
Line	**Any**					**Any**
N	17					15
ORR, %	25 %					47 %
DCR, %	43.8 %					53 %
Median PFS, mo (95% CI)	2.1 (0.5 – 4.9)					12.6 (1.9 – Not reached)
Median OS, mo (95% CI)	2.8 (0.9 – 6.9)					14.6 (4.6 – Not reached)
PD-L1	**≥ 50%**		**≥ 50%**	**≥ 50%**	**≥ 50%**	
Line	**First**		**First**	**First**	**First**	
N	12		153	39	56	
ORR, %	27.3 %		21 %	25.6 %	45 %	
DCR, %	45.5 %		37 %	Not reported	Not reported	
Median PFS, mo (95% CI)	2.1 (0.5 – 4.9)		2.4 (1.6 – 2.5)	4.0 (2.07 – 14.04)	2.6 (1.9 – 5.1)	
Median OS, mo (95% CI)	2.8 (0.5 – 6.9)		3.0 (2.4 – 3.5)	7.4 (3.78 – Not reached)	7.8 (2.5 – 10.7)	

Abbreviations: ECOG PS = Eastern Cooperative Oncology group performance status, DCR = Disease control rate, mo = months, ORR = Overall response rate, OS = Overall survival, N = Number of patients, NSCLC = Non-small cell lung cancer, PD-L1 = Programmed death ligand-1, PFS = Progression-free survival, TPS = Tumor proportion score

eTable 4. Clinicopathologic and Treatment Characteristics of Patients With ECOG PS of at Least 2 With or Without Durable Clinical Benefit

		Durable Clinical Benefit (N = 7)	No Durable Clinical Benefit (N = 22)	P value
ECOG PS	2, n (%) 3, n (%)	6 (85.7) 1 (14.3)	19 (86.4) 3 (13.6)	1.00
Age, years	Median (range)	68 (63 – 87)	72.5 (42 – 86)	0.68
Sex	Female, n (%)	3 (42.9)	11 (50)	1.00
Race	Caucasian, n (%) African American, n (%) Asian, n (%)	5 (71.4) 2 (28.6) 0	16 (72.7) 4 (18.2) 2 (9.1)	0.79
Body Mass Index	Median (range)	25.3 (19.5 – 37.3)	24.9 (17.3 – 40.9)	0.58
Obesity	Yes, n (%)	3 (42.9)	5 (22.7)	0.36
Smoking	Ever, n (%)	7 (100)	18 (81.8)	0.55
Comorbidities	Simplified Comorbidity Score, Median (range) Hypertension, n (%) Diabetes mellitus, n (%) Cardiovascular, n (%) Respiratory, n (%) Creatinine clearance <60, n (%) Creatinine clearance <30, n (%) VTE, n (%)	9 (7 – 13) 3 (42.9) 0 (0) 3 (42.9) 4 (57.1) 3 (42.9) 0 (0) 1 (14.3)	9 (2 – 14) 14 (63.6) 4 (18.2) 6 (27.3) 8 (36.4) 8 (36.4) 1 (4.5) 5 (22.7)	0.88 0.40 0.55 0.64 0.40 1.00 1.00 1.00
Histology	Non-squamous, n (%) Squamous, n (%) Poorly differentiated, n (%)	5 (71.4) 2 (28.6) 0	14 (63.6) 6 (27.3) 2 (9.1)	1.00
Driver mutations/ alterations (N=26 [7/19])	None, n (%) KRAS, n (%) EGFR, n (%) Others, n (%) - MET, n (%) - BRAF, n (%)	4 (57.1) 2 (28.6) 1 (14.3) 0 0 0	6 (31.6) 10 (52.6) 1 (5.3) 2 (10.5) 1 (5.3) 1 (5.3)	0.38
PD-L1 TPS	Median (range) ≥ 50%, n (%)	40 (1 – 100) 3 (42.9)	70 (1 – 90) 14 (63.6)	0.30 0.40
Sites of metastases	Number, Median (range) Lung/pleura, n (%) Lymph node, n (%) Brain, n (%)	2 (1 – 4) 5 (71.4) 3 (42.9) 1 (14.3)	2 (1 – 5) 12 (54.5) 12 (54.5) 8 (36.4)	0.22 0.67 0.68 0.38

	Bone, n (%) Liver, n (%) Adrenal, n (%) Others, n (%)	3 (42.9) 0 (0) 1 (14.3) 1 (14.3)	13 (59.1) 4 (18.2) 3 (13.6) 7 (31.8)	0.67 0.55 1.00 0.64
Line of therapy	First line, n (%) ≥ Second line, n (%)	6 (85.7) 1 (14.3)	15 (68.2) 7 (31.8)	0.64
WBC (K/uL)	Median (range)	7.9 (5.4 – 10.2)	8.6 (4.7 – 37.5)	0.40
ANC (K/uL)	Median (range)	5.59 (3.38 – 7.52)	6.92 (3.51 – 22.4)	0.25
Creatinine (mg/dL)	Median (range)	0.9 (0.4 – 1.8)	0.85 (0.5 – 2.3)	0.74
Objective response (N=28 [7/21])	ORR, n (%) • CR, n (%) • PR, n (%)	4 (57.1) 0 (0) 4 (57.1)	1 (4.8) 0 (0) 1 (4.8)	0.008
Immune-related adverse events	Any grade, n (%) ≥ Grade 3, n (%) Steroid use, n (%)	5 (71.4) 1 (14.3) 1 (14.3)	4 (18.2) 4 (18.2) 4 (18.2)	0.02 1.00 1.00

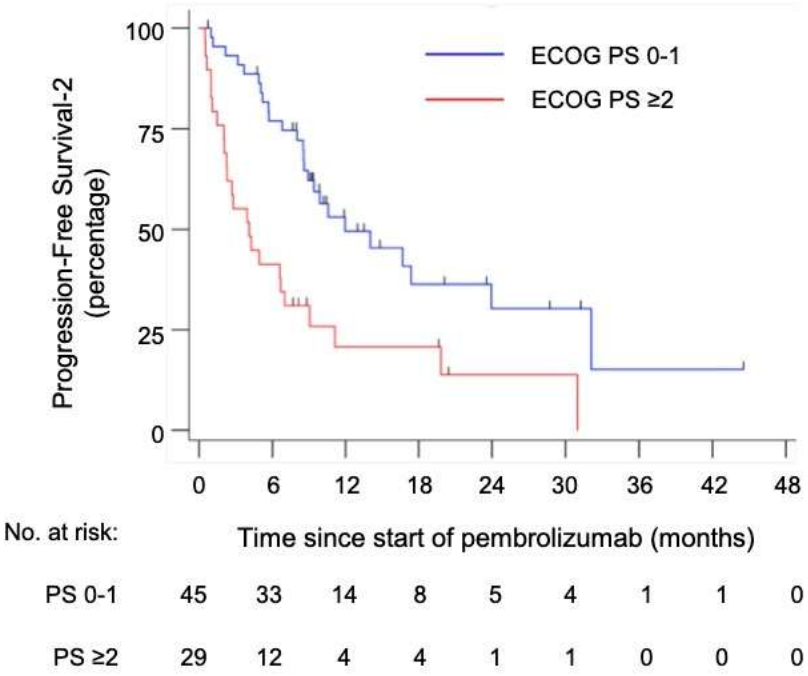
Abbreviations: ANC = Absolute neutrophil count, CAD = Coronary artery disease, CHF = Congestive heart failure, CR = Complete response, ECOG PS = Eastern Cooperative Oncology group performance status, K/uL = x1000/microliter, ORR = Overall response rate, PD-L1 = Programmed death ligand 1, PR = Partial response, TPS = Tumor proportion score, VTE = Venous thromboembolic disease, WBC = White blood cell count, wk = weeks

eTable 5. Treatment Outcomes in Patients With ECOG PS 0-1 vs ECOG PS2

		All (N = 70)	ECOG PS 0-1 (N = 45)	ECOG PS =2 (N = 25)	P value
Objective response (N=67 [43/24])	ORR, n (%) • CR, n (%) • PR, n (%)	16 (23.9) 2 (2.9) 14 (20.9)	12 (27.9) 2 (4.6) 10 (23.3)	4 (16.7) 0 (0) 4 (16.7)	0.38
Disease control (N=67 [43/24])	DCR, n (%) • SD, n (%)	51 (76.1) 35 (52.2)	38 (88.4) 26 (60.5)	13 (54.2) 9 (37.5)	0.003
Immune-related adverse events	Any grade, n (%) ≥ Grade 3, n (%) Steroid use, n (%) Treatment discontinuation, n (%) Death, n (%)	32 (45.7) 11 (15.7) 15 (21.4) 7 (10) 1 (1.4)	24 (53.3) 6 (13.3) 10 (22.2) 3 (6.7) 1 (2.2)	8 (32) 5 (20) 5 (20) 4 (16) 0 (0)	0.09 0.51 1.00 0.24 1.00
Progression Free Survival	Median, months (95% CI)	4.9 (3.3 – 7.9)	7.9 (4.6 – 15.4)	2.3 (1.8 – 4.8)	0.003
Progression Free Survival-2	Median, months (95% CI)	8.9 (6.6 – 11.9)	11.9 (8.6 – 23.9)	4.1 (2.3 – 6.9)	<0.001
Overall Survival	Median, months (95% CI)	12.7 (6.7 – 23.2)	23.2 (14.0 – 35.7)	4.1 (2.3 – 6.9)	<0.001
Death on home hospice	Yes, n (%) No, n (%) Not known, n (%) Not applicable, n (%)	26 (37.1) 14 (20) 2 (2.9) 28 (40)	15 (33.3) 7 (15.6) 0 (0) 23 (51.1)	11 (44) 7 (28) 2 (8) 5 (20)	0.35

Abbreviations: CR = Complete response, DCR = Disease control rate, ECOG PS = Eastern Cooperative Oncology group performance status, ORR = Overall response rate, PR = Partial response, SD = Stable disease

eFigure 1. Univariate Kaplan-Meier Survival Curves for Progression-Free Survival-2 in Patients With Advanced NSCLC and ECOG PS 0-1 vs at Least 2 Treated With Pembrolizumab Monotherapy



No. at risk:									
PS 0-1	45	33	14	8	5	4	1	1	0
PS ≥2	29	12	4	4	1	1	0	0	0

eFigure 2. Univariate Kaplan-Meier Survival Curves for Progression-Free Survival, Overall Survival, and Progression-Free Survival in Patients With Advanced NSCLC and ECOG PS 0-1 vs 2 Treated With Pembrolizumab Monotherapy