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Supplemental data

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Sabatolimab in combination with spartalizumab in patients with non-small cell lung cancer or melanoma who received prior treatment with anti-PD-1/PD-L1 therapy : a phase 2 multicentre study

Lin, Chia-Chi; Curigliano, Giuseppe; Santoro, Armando; Kim, Dong-Wan; Tai, David; Hodi, F Stephen; Wilgenhof, Sofie; Doi, Toshihiko; Sabatos-Peyton, Catherine; Szpakowski, Sebastian; Chitnis, Shripad; Xyrafas, Alexandros; Gutzwiller, Sabine; Pastore, Alessandro [**and 1 more**]

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SUPPLEMENTAL MATERIAL

Supplemental Table S1. Study centers and ethics committee or institutional review board

Center Number	Ethics Committee or Institutional Review Board	Location
1000	METC Leiden-Den Haag-Delft	Holland, Netherlands
1001	METC Leiden-Den Haag-Delft	Holland, Netherlands
1100	Commission Cantonale d'Éthique de la Recherche (CCER)	Geneva, Switzerland
1300	Comitato Etico degli IRCCS Istituto Europeo di Oncologia e Centro Cardiologico Monzino	Milano, Italy
1301	Comitato Etico Dell'IRCCS Istituto Clinico Humanitas	Milano, Italy
2100	Singhealth Centralized Institutional Review Board	Singapore, Singapore
2200	National Taiwan University Hospital IRB	Taipei, Taiwan
2300	Seoul National University College of Medicine/ Seoul National University Hospital Institutional Review Board	Seoul, South Korea
3000	University Health Network REB	Ontario, Canada
4000	Institutional Review Board of National Cancer Center	Tokyo, Japan
5000	Dana-Farber Cancer Institute IRB	Boston, Massachusetts, USA
5001	The University of Texas MD Anderson Cancer Center Institutional Review Board	Houston, Texas, USA
5002	UT Health San Antonio IRB	San Antonio, Texas, USA
5003	The Johns Hopkins Institutional Review Board	Baltimore, Maryland, USA

Supplemental Table S2. Baseline patient demographics and characteristics by indication

Characteristic	Melanoma (N=16) ^a	NSCLC (N=17)	All Patients (N=33)
Median age, years (range)	64.0 (42-78)	69.0 (46-78)	66.0 (42-78)
Sex, n (%)			
Female	8 (50.0)	3 (17.6)	11 (33.3)
Male	8 (50.0)	14 (82.4)	22 (66.7)
Race, n (%)			
Caucasian	8 (50.0)	11 (64.7)	19 (57.6)
Asian	8 (50.0)	5 (29.4)	13 (39.4)
Other	0	1 (5.9)	1 (3.0)
ECOG performance status, n (%)			
0	9 (56.3)	4 (23.5)	13 (39.4)
1	7 (43.8)	11 (64.7)	18 (54.5)
2	0	2 (11.8)	2 (6.1)
Primary site of melanoma, n (%)			
Cutaneous	14 (87.5)	-	14 (42.4)
Non-cutaneous	1 (6.3)	-	1 (3.0)
Uveal	1 (6.3)	-	1 (3.0)
Predominant tumor histology/cytology, NSCLC, n (%)			
Adenocarcinoma	-	10 (58.8)	10 (30.3)
Squamous cell carcinoma	-	7 (41.2)	7 (21.2)
Clinical benefit of prior anti-PD-1/PD-L1 therapy ^b , n (%)			
DCB	6 (37.5)	7 (41.2)	13 (39.4)
NDCB	10 (62.5)	9 (52.9)	19 (57.6)
Unknown	0	1 (5.9)	1 (3.0)
Immediate ^c prior PD-1/PD-L1 therapy, n (%)			
Yes	10 (62.5)	11 (64.7)	21 (63.6)
No	6 (37.5)	6 (35.3)	12 (36.4)
Prior immune checkpoint inhibitor therapy, n (%)			
Yes	15 (93.8)	15 (88.2)	30 (90.9)
No	1 (6.3)	2 (11.8)	3 (9.1)

DCB, durable clinical benefit (best response of complete or partial response, or stable disease for ≥ 6 months); ECOG, Eastern Cooperative Oncology Group; NDCB, non-durable clinical benefit (best response of progressive disease or stable disease for < 6 months); NSCLC, non-small cell lung cancer; PD-1, programmed death 1; PD-L1, programmed death ligand 1.

^a14 patients with cutaneous melanoma, and 1 patient each with non-cutaneous and uveal melanoma.

^bClinical benefit of prior anti-PD-1/PD-L1 therapy was defined as durable if patients had as best response of complete or partial response, or stable disease for ≥ 6 months (DCB), or non-durable if patients had as best response progressive disease or stable disease for < 6 months (NDCB).

^cImmediate: Last therapy before receiving sabatolimab plus spartalizumab.

Supplemental Table S3. Adverse events regardless of study treatment relationship (≥5% of patients)

Preferred Term	Melanoma (N=16)		NSCLC (N=17)		All Patients (N=33)	
	All Grades n (%)	Grade ≥3 n (%)	All Grades n (%)	Grade ≥3 n (%)	All Grades n (%)	Grade ≥3 n (%)
Number of patients with at least 1 event	15 (93.8)	5 (31.3)	16 (94.1)	10 (58.8)	31 (93.9)	15 (45.5)
Fatigue	4 (25).0	0	4 (23.5)	1 (5.9)	8 (24.2)	1 (3.0)
Nausea	5 (31.3)	0	3 (17.6)	0	8 (24.2)	0
Anemia	2 (12.5)	0	4 (23.5)	2 (11.8)	6 (18.2)	2 (6.1)
Cough	3 (18.8)	0	3 (17.6)	0	6 (18.2)	0
Pyrexia	2 (12.5)	0	4 (23.5)	0	6 (18.2)	0
Constipation	1 (6.3)	0	4 (23.5)	0	5 (15.2)	0
Dyspnea	1 (6.3)	0	4 (23.5)	2 (11.8)	5 (15.2)	2 (6.1)
Vomiting	3 (18.8)	0	2 (11.8)	0	5 (15.2)	0
Abdominal pain	1 (6.3)	0	3 (17.6)	1 (5.9)	4 (12.1)	1 (3.0)
Diarrhea	1 (6.3)	0	3 (17.6)	0	4 (12.1)	0
Alanine aminotransferase increased	1 (6.3)	0	2 (11.8)	1 (5.9)	3 (9.1)	1 (3.0)
Asthenia	1 (6.3)	0	2 (11.8)	1 (5.9)	3 (9.1)	1 (3.0)
Decreased appetite	2 (12.5)	0	1 (5.9)	0	3 (9.1)	0
Musculoskeletal pain	0	0	3 (17.6)	0	3 (9.1)	0
Pruritus	2 (12.5)	0	1 (5.9)	1 (5.9)	3 (9.1)	1 (3.0)
Abdominal pain upper	1 (6.3)	0	1 (5.9)	0	2 (6.1)	0
Arthralgia	1 (6.3)	0	1 (5.9)	0	2 (6.1)	0
Aspartate aminotransferase increased	1 (6.3)	0	1 (5.9)	0	2 (6.1)	0

Preferred Term	Melanoma (N=16)		NSCLC (N=17)		All Patients (N=33)	
	All Grades n (%)	Grade ≥3 n (%)	All Grades n (%)	Grade ≥3 n (%)	All Grades n (%)	Grade ≥3 n (%)
Back pain	0	0	2 (11.8)	0	2 (6.1)	0
General physical health deterioration	1 (6.3)	1 (6.3)	1 (5.9)	1 (5.9)	2 (6.1)	2 (6.1)
Hemoptysis	1 (6.3)	0	1 (5.9)	0	2 (6.1)	0
Hypokalemia	2 (12.5)	1 (6.3)	0	0	2 (6.1)	1 (3.0)
Hypophosphatemia	1 (6.3)	1 (6.3)	1 (5.9)	0	2 (6.1)	1 (3.0)
Pain in extremity	2 (12.5)	0	0	0	2 (6.1)	0
Paresthesia	2 (12.5)	0	0	0	2 (6.1)	0
Pneumonia	0	0	2 (11.8)	2 (11.8)	2 (6.1)	2 (6.1)
Sinus tachycardia	0	0	2 (11.8)	0	2 (6.1)	0
Stomatitis	1 (6.3)	0	1 (5.9)	1 (5.9)	2 (6.1)	1 (3.0)
White blood cell count decreased	2 (12.5)	0	0	0	2 (6.1)	0
Amylase increased	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Anxiety	0	0	1 (5.9)	0	1 (3.0)	0
Aspartate aminotransferase	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Blood alkaline phosphatase increased	0	0	1 (5.9)	0	1 (3.0)	0
Blood bilirubin increased	1 (6.3)	0	0	0	1 (3.0)	0
Blood calcium increased	0	0	1 (5.9)	0	1 (3.0)	0
Blood creatinine increased	0	0	1 (5.9)	0	1 (3.0)	0
Bronchial obstruction	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Cellulitis	1 (6.3)	0	0	0	1 (3.0)	0

Preferred Term	Melanoma (N=16)		NSCLC (N=17)		All Patients (N=33)	
	All Grades n (%)	Grade ≥3 n (%)	All Grades n (%)	Grade ≥3 n (%)	All Grades n (%)	Grade ≥3 n (%)
Chills	0	0	1 (5.9)	0	1 (3.0)	0
Chronic obstructive pulmonary disease	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Colitis	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Contrast media allergy	0	0	1 (5.9)	0	1 (3.0)	0
Dehydration	1 (6.3)	0	0	0	1 (3.0)	0
Dermatophytosis of nail	1 (6.3)	0	0	0	1 (3.0)	0
Diabetes mellitus	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Dizziness	0	0	1 (5.9)	0	1 (3.0)	0
Ear pain	1 (6.3)	0	0	0	1 (3.0)	0
Ecchymosis	1 (6.3)	0	0	0	1 (3.0)	0
Face edema	0	0	1 (5.9)	0	1 (3.0)	0
Flank pain	1 (6.3)	0	0	0	1 (3.0)	0
Foreign body sensation in eyes	0	0	1 (5.9)	0	1 (3.0)	0
Hematuria	1 (6.3)	0	0	0	1 (3.0)	0
Headache	1 (6.3)	0	0	0	1 (3.0)	0
Hypercalcemia	0	0	1 (5.9)	0	1 (3.0)	0
Hyperthyroidism	0	0	1 (5.9)	0	1 (3.0)	0
Hyponatremia	1 (6.3)	0	0	0	1 (3.0)	0
Hypovitaminosis	0	0	1 (5.9)	0	1 (3.0)	0
Influenza-like illness	1 (6.3)	0	0	0	1 (3.0)	0

Preferred Term	Melanoma (N=16)		NSCLC (N=17)		All Patients (N=33)	
	All Grades n (%)	Grade ≥3 n (%)	All Grades n (%)	Grade ≥3 n (%)	All Grades n (%)	Grade ≥3 n (%)
International normalized ratio increased	0	0	1 (5.9)	0	1 (3.0)	0
Jugular vein thrombosis	0	0	1 (5.9)	0	1 (3.0)	0
Lethargy	0	0	1 (5.9)	0	1 (3.0)	0
Lip infection	0	0	1 (5.9)	0	1 (3.0)	0
Lipase increased	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Lower respiratory tract infection bacterial	0	0	1 (5.9)	0	1 (3.0)	0
Lymphocyte count decreased	0	0	1 (5.9)	0	1 (3.0)	0
Lymphopenia	0	0	1 (5.9)	0	1 (3.0)	0
Mouth ulceration	1 (6.3)	0	0	0	1 (3.0)	0
Musculoskeletal chest pain	1 (6.3)	0	0	0	1 (3.0)	0
Myalgia	1 (6.3)	0	0	0	1 (3.0)	0
Neck pain	1 (6.3)	0	0	0	1 (3.0)	0
Non-cardiac chest pain	0	0	1 (5.9)	0	1 (3.0)	0
Oral fungal infection	0	0	1 (5.9)	0	1 (3.0)	0
Oropharyngeal pain	1 (6.3)	0	0	0	1 (3.0)	0
Pathological fracture	1 (6.3)	1 (6.3)	0	0	1 (3.0)	1 (3.0)
Platelet count decreased	1 (6.3)	0	0	0	1 (3.0)	0
Pleural effusion	0	0	1 (5.9)	0	1 (3.0)	0
Psoriasis	1 (6.3)	0	0	0	1 (3.0)	0
Rash	1 (6.3)	0	0	0	1 (3.0)	0

Preferred Term	Melanoma (N=16)		NSCLC (N=17)		All Patients (N=33)	
	All Grades n (%)	Grade ≥3 n (%)	All Grades n (%)	Grade ≥3 n (%)	All Grades n (%)	Grade ≥3 n (%)
Rhinitis allergic	1 (6.3)	0	0	0	1 (3.0)	0
Seborrheic dermatitis	1 (6.3)	0	0	0	1 (3.0)	0
Skin infection	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Speech disorder	1 (6.3)	0	0	0	1 (3.0)	0
Superior vena cava syndrome	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Swelling	1 (6.3)	0	0	0	1 (3.0)	0
Tumor invasion	1 (6.3)	1 (6.3)	0	0	1 (3.0)	1 (3.0)
Venous thrombosis	0	0	1 (5.9)	0	1 (3.0)	0
Vertigo	0	0	1 (5.9)	0	1 (3.0)	0
Weight decreased	1 (6.3)	0	0	0	1 (3.0)	0

NSCLC, non-small cell lung cancer.

Table S4. Adverse events suspected to be related to study treatment ($\geq 2\%$ of patients)

Preferred Term	Melanoma (N=16)		NSCLC (N=17)		All Patients (N=33)	
	All Grades n (%)	Grade ≥ 3 n (%)	All Grades n (%)	Grade ≥ 3 n (%)	All Grades n (%)	Grade ≥ 3 n (%)
Number of patients with at least 1 event	9 (56.3)	0	6 (35.3)	2 (11.8)	15 (45.5)	2 (6.1)
Fatigue	1 (6.3)	0	2 (11.8)	0	3 (9.1)	0
Nausea	1 (6.3)	0	2 (11.8)	0	3 (9.1)	0
Pruritus	2 (12.5)	0	1 (5.9)	1 (5.9)	3 (9.1)	1 (3.0)
Alanine aminotransferase increased	1 (6.3)	0	1 (5.9)	1 (5.9)	2 (6.1)	1 (3.0)
Anemia	1 (6.3)	0	1 (5.9)	0	2 (6.1)	0
Aspartate aminotransferase increased	1 (6.3)	0	1 (5.9)	0	2 (6.1)	0
Asthenia	1 (6.3)	0	1 (5.9)	0	2 (6.1)	0
Abdominal pain upper	0	0	1 (5.9)	0	1 (3.0)	0
Amylase increased	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Chills	0	0	1 (5.9)	0	1 (3.0)	0
Diarrhea	0	0	1 (5.9)	0	1 (3.0)	0
Dyspnea	1 (6.3)	0	0	0	1 (3.0)	0
Hypovitaminosis	0	0	1 (5.9)	0	1 (3.0)	0
Lipase increased	0	0	1 (5.9)	1 (5.9)	1 (3.0)	1 (3.0)
Psoriasis	1 (6.3)	0	0	0	1 (3.0)	0
Pyrexia	1 (6.3)	0	0	0	1 (3.0)	0
Rash	1 (6.3)	0	0	0	1 (3.0)	0
Vomiting	0	0	1 (5.9)	0	1 (3.0)	0

NSCLC, non-small cell lung cancer.

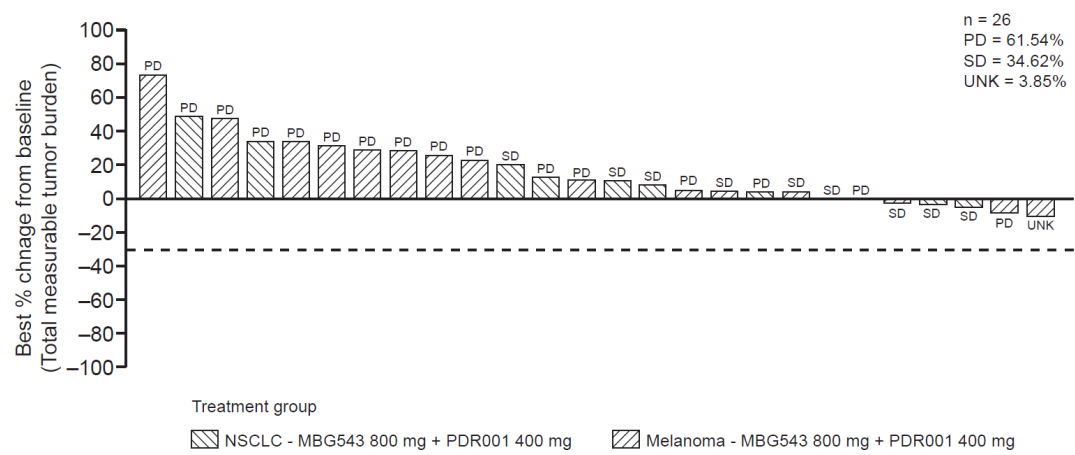
Supplemental Table S5. Sabatolimab PK parameters for sabatolimab plus spartalizumab

Schedule/Parameter	Melanoma	NSCLC	All Patients
Cycle 1			
AUC _{tau} (day*µg/mL)	2500 (930)	1720 (709)	2100 (901)
n	16	13	22
C _{max} (µg/mL)	229 (59.9)	180 (62.8)	204 (65.5)
n	16	17	33
Cycle 3			
AUC _{tau} (day*µg/mL)	4900 (1250)	3150 (1370)	3960 (1550)
n	6	7	13
C _{max} (µg/mL)	316 (105)	263 (85)	291 (97.3)
n	9	8	17
T _{1/2} (days)	21.7 (2.14)	19.1 (8.69)	20.3 (6.45)
n	6	7	13

AUC_{tau}, area under the plasma concentration-time curve for a dosing interval; C_{max}, maximum plasma concentration; NSCLC, non-small cell lung cancer; PK, pharmacokinetics; T_{1/2}, half-life.

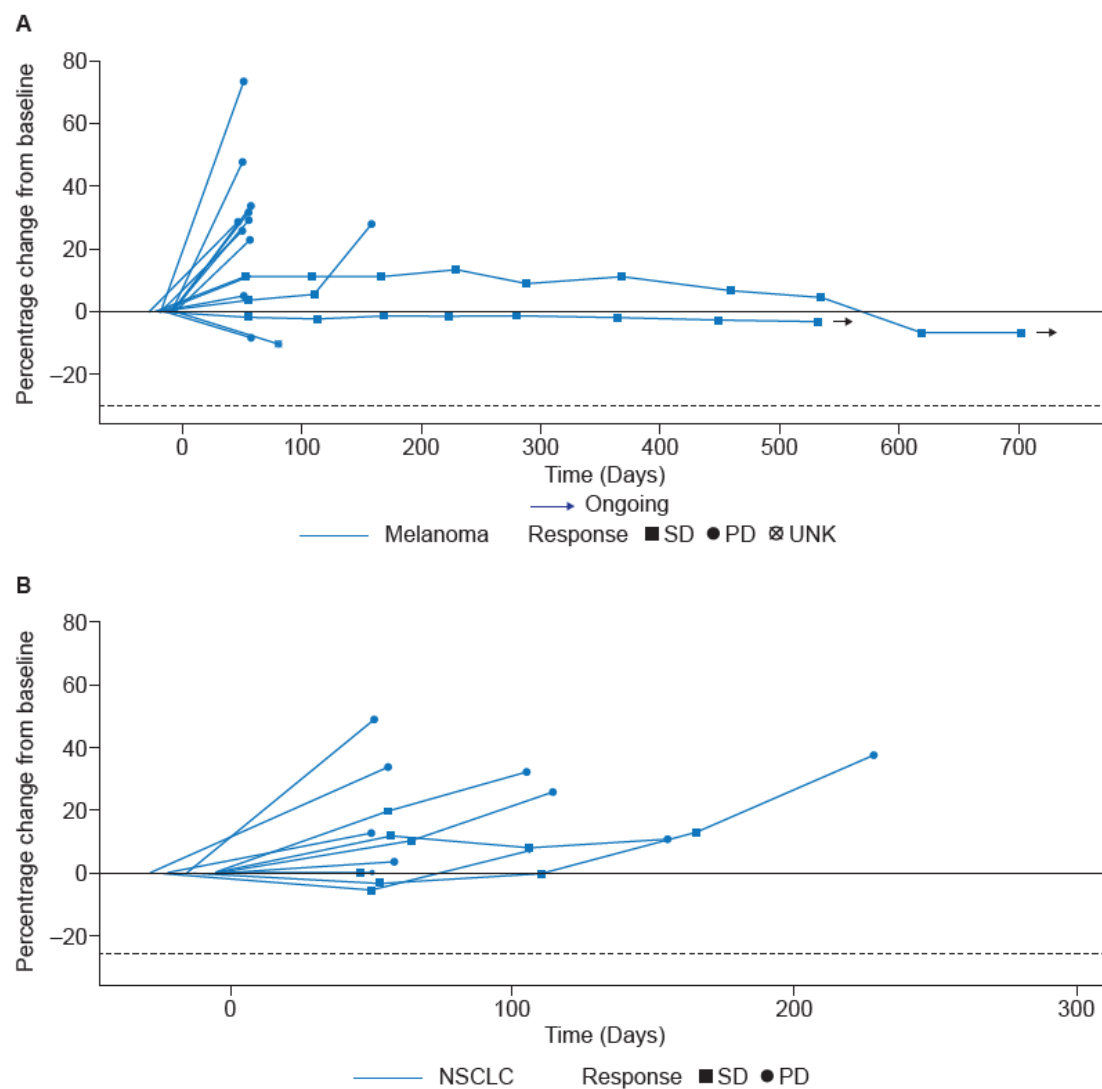
Supplemental Table S6. Dose received of sabatolimab and spartalizumab

	Melanoma	NSCLC	All Patients
Sabatolimab			
Average 4-weekly dose (mg), mean (SD)	800.00 (0.000)	772.94 (62.826)	786.06 (46.499)
Cumulative dose (mg), mean (SD)	3950.0 (4768.51)	2541.2 (1838.16)	3224.2 (3586.00)
Dose intensity (mg/28 days), mean (SD)	802.10 (12.792)	773.58 (57.616)	787.41 (44.114)
Relative dose intensity (%)	100.27 (1.609)	96.70 (7.203)	98.43 (5.517)
Spartalizumab			
Average 4-weekly dose (mg), mean (SD)	400.00 (0.000)	386.47 (31.413)	393.03 (23.249)
Cumulative dose (mg), mean (SD)	1975.0 (2384.25)	1270.6 (919.08)	1612.1 (1793.00)
Dose intensity (mg/28 days), mean (SD)	401.05 (6.396)	386.79 (28.808)	393.71 (22.057)
Relative dose intensity (%)	100.27 (1.609)	96.70 (7.203)	98.43 (5.517)



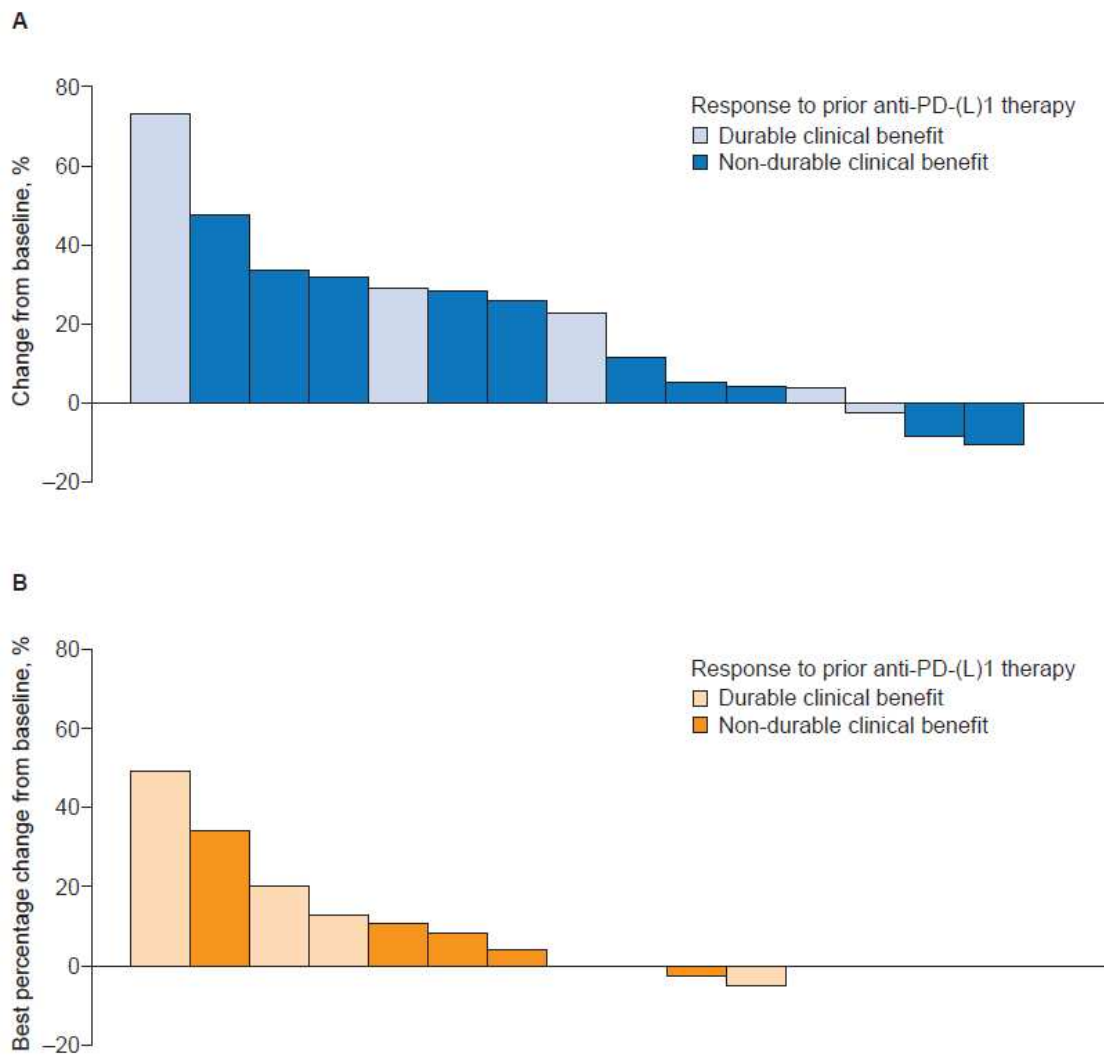
Supplemental Figure S1. Best percentage change from baseline in sum of diameters of target lesions based on local radiology review per RECIST v1.1.

NSCLC, non-small cell lung cancer; PD, progressive disease; RECIST, Response Evaluation Criteria In Solid Tumors; SD, stable disease; UNK, unknown.

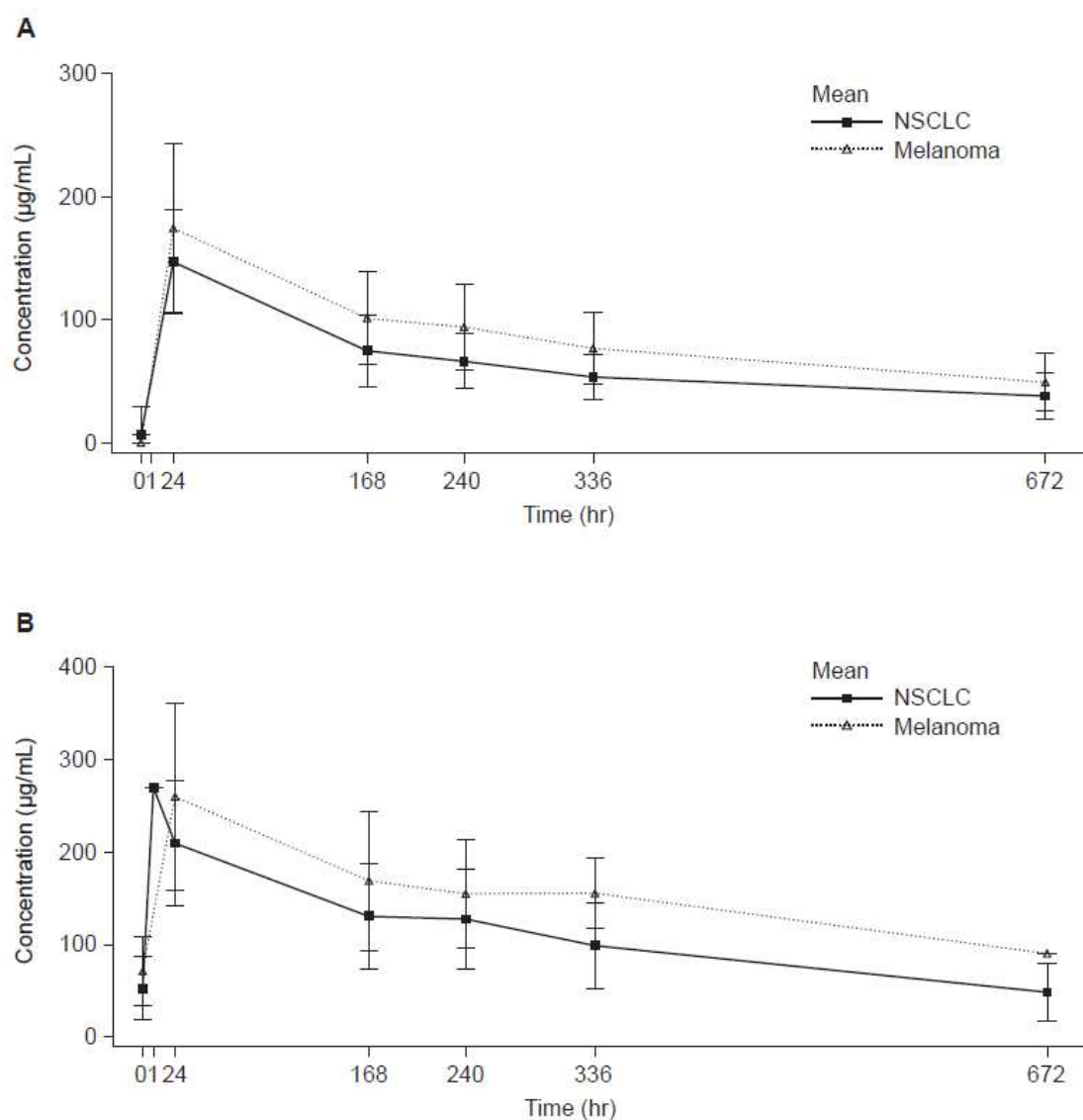


Supplemental Figure S2. Percentage change from baseline in target lesions over time for patients with (A) melanoma and (B) NSCLC.

NSCLC, non-small cell lung cancer; PD, progressive disease; SD, stable disease; UNK, unknown.



Supplemental Figure S3. Best percentage change from baseline of target lesions, by response to prior anti-PD-1/PD-L1 therapy for patients with (A) melanoma or (B) NSCLC. NSCLC, non-small cell lung cancer; PD-1, programmed death 1; PD-L1, programmed death ligand 1.



Supplemental Figure S4. Sabatolimab mean concentration–time profiles for sabatolimab $\pm$ spartalizumab in Cycle 1 (A) and Cycle 3 (B), by indication. NSCLC, non-small cell lung cancer.