THE LANCET Oncology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Kwon ED, Drake CG, Scher HI, et al, for the CA184-043 Investigators. Ipilimumab versus placebo after radiotherapy in patients with metastatic castration-resistant prostate cancer that had progressed after docetaxel chemotherapy (CA184-043): a multicentre, randomised, double-blind, phase 3 trial. *Lancet Oncol* 2014; published online May 13. http://dx.doi.org/10.1016/S1470-2045(14)70189-5.

Appendix

Supplementary Table 1: Subsequent systemic anticancer treatments

	Ipilimumab (n=393), %	Placebo (n=396), %
Overall	41.0	46.7
Abiraterone	21.1	21.8
Cabazitaxel	13.0	16.6
Docetaxel	6.0	6.1
Mitoxantrone	6.1	7.8
Carboplatin	3.0	2.0
Cyclophosphamide	2.5	3.5
Enzalutamide	2.0	1.3

Supplementary Table 2: Multivariate analysis of OS for baseline prognostic features*

Prognostic feature	Comparison	P value**	HR (95% CI)
Treatment	Ipilimumab vs placebo	0.0408	0.81 (0.66–0.99)
Age	≥70 vs <70 years	0.0100	1.30 (1.07–1.60)
Log (ALP)	Continuous variable	<0.0001	1.40 (1.24–1.58)
Log (PSA)	Continuous variable	<0.0001	1.16 (1.08–1.24)
Visceral metastases	Yes vs No	0.0024	1.40 (1.13–1.73)
Hemoglobin	≥11 g/dL vs <11 g/dL	<0.0001	0.54 (0.43–0.67)
Average daily worst pain intensity	≥4 vs <4	0.0030	1.37 (1.11–1.68)
Bone regions with metastases	≥2 vs 1	0.0053	1.38 (1.10–1.73)

*Sensitivity analysis of OS; the Cox regression multivariate model (intention-to-treat population) was pre-specified. A threshold ≤0.1 was used to determine if the pre-specified baseline feature was to be included in the model. No multiplicity adjustment.

**For exploratory purposes only.

ALP, alkaline phosphatase.

Supplementary Table 3: Prespecified secondary and exploratory endpoints

Endpoint	Ipilimumab (N = 399)	Placebo (N = 400)	Hazard Ratio (95% CI)	P Value
Secondary				
PFS* (months)	4.0 (3.6–4.3)	3.1 (2.9–3.4)	0.70 (0.61–0.82)	<0.0001†
Pain response‡ (%)	3.6 (1.44–7.18)	0.5 (0.01–2.96)	NA	
Exploratory				
PSA response rate§ (%)	13.1(9.5–17.5)	5.2 (3.0–8.4)	NA	

*PFS was a composite endpoint based on PSA progression, radiological progression, clinical deterioration, or death. PSA progression was defined as a PSA increase of ≥25% and ≥2 ng/ml above the nadir on or after week 12, confirmed over 2 subsequent assessments. Radiological progression was defined as progression in target, non-target (non-bone), or bone lesions on or after week 12 and confirmed by assessment performed at least 6 weeks later. Clinical deterioration was defined as a) persistent decrease in performance status (e.g., lasting >14 days) of at least 2 points from baseline, attributable to disease progression; OR b) any symptomatic clinical event due to disease progression that indicated that the patient was not benefiting from study treatment AND could not be managed by supportive care (such as bisphosphonates and/or bone-directed RT); c) any change of antineoplastic therapy due to prostate cancer.

†Interpretation for descriptive purposes only.

‡Pain response was defined as a decrease in average daily worst pain intensity (Question #3 on the Brief Pain Inventory Short Form) by ≥30% from baseline, maintained over 2 consecutive assessments, without any rescue medication or increase in analgesic use in the same time period. Percentage shown as ratio of number of pain responders/number of pain evaluable patients; 7/197 and 1/186 in ipilimumab and placebo arms, respectively.

§PSA response was defined as a decrease from baseline of 50%, which was confirmed by a second PSA value 6 weeks later. PSA change from baseline was analyzed over time. Percentage shown as ratio of number of PSA responders/number of PSA response evaluable patients; 39/297 and 16/305 in ipilimumab and placebo arms, respectively.

NA=not applicable. PFS=progression-free survival. PSA=prostate-specific antigen.

Supplementary Table 4: On-study adverse events

	Ipilimumab (n=393)				Placebo (n=396)			
	Any grade	**Grade 3**	**Grade 4**	**Grade 5**	**Any grade**	**Grade 3**	**Grade 4**	**Grade 5**
Any event*	385 (98.0)	190 (48.3)	42 (10.7)	66 (16.8)	364 (91.9)	117 (29.5)	45 (11.4)	45 (11.4)
Gastrointestinal disorders	285 (72.5)	85 (21.6)	6 (1.5)	3 (0.8)	224 (56.6)	33 (8.3)	0	0
Diarrhea	199 (50.6)	63 (16.0)	1 (0.3)	0	97 (24.5)	7 (1.8)	0	0
Nausea	127 (32.3)	11 (2.8)	0	0	106 (26.8)	7 (1.8)	0	0
Vomiting	111 (28.2)	7 (1.8)	0	0	85 (21.5)	9 (2.3)	0	0
Constipation	69 (17.6)	2 (0.5)	0	0	83 (21.0)	3 (0.8)	0	0
Abdominal pain	36 (9.2)	6 (1.5)	0	0	26 (6.6)	7 (1.8)	0	0
Colitis	27 (6.9)	15 (3.8)	3 (0.8)	0	3 (0.8)	0	0	0
Abdominal pain (upper)	14 (3.6)	1 (0.3)	0	0	17 (4.3)	2 (0.5)	0	0
Gastritis	11 (2.8)	4 (1.0)	0	0	4 (1.0)	0	0	0
Hemorrhoids	8 (2.0)	0	0	0	8 (2.0)	1 (0.3)	0	0
Abdominal distention	5 (1.3)	1 (0.3)	0	0	5 (1.3)	0	0	0
Rectal hemorrhage	3 (0.8)	0	0	0	5 (1.3)	1 (0.3)	0	0
Ulcerative colitis	2 (0.5)	1 (0.3)	1(0.3)	0	0	0	0	0
Gastrointestinal disorder	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Gastrointestinal hemorrhage	2 (0.5)	0	0	1 (0.3)	0	0	0	0
Intestinal hemorrhage	2 (0.5)	0	1 (0.3)	0	0	0	0	0
Large intestine perforation	2 (0.5)	2 (0.5)	0	0	0	0	0	0
Proctocolitis	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Proctalgia	1 (0.3)	0	0	0	2 (0.5)	1 (0.3)	0	0
Diverticular perforation	1 (0.3)	0	0	1 (0.3)	0	0	0	0
Abdominal tenderness	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Diaphragmatic hernia	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Fecaloma	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Femoral hernia, obstructive	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Gastric ileus	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Gastric ulcer	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Gastric atrophic	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Gastrointestinal obstruction	1 (0.3)	1 (0.3)	0	0	1 (0.3)	1 (0.3)	0	0

Gastrointestinal pain	1 (0.3)	1 (0.3)	0	0	1 (0.3)	1 (0.3)	0	0
Hematochezia	1 (0.3)	1 (0.3)	0	0	1 (0.3)	0	0	0
Ileitis	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Intestinal obstruction	1 (0.3)	0	0	1 (0.3)	1 (0.3)	1 (0.3)	0	0
General disorders	266 (67.7)	74 (18.8)	12 (3.1)	7 (1.8)	255 (64.4)	65 (16.4)	7 (1.8)	7 (1.8)
Fatigue	150 (38.2)	34 (8.7)	6 (1.5)	0	123 (31.1)	31 (7.8)	4 (1.0)	0
Pyrexia	89 (22.6)	5 (1.3)	0	0	51 (12.9)	1 (0.3)	0	0
Asthenia	82 (20.9)	25 (6.4)	1 (0.3)	0	68 (17.2)	12 (3.0)	1 (0.3)	0
Peripheral edema	51 (13.0)	0	0	0	37 (9.3)	2 (0.5)	0	0
Pain	37 (9.4)	8 (2.0)	2 (0.5)	0	49 (12.4)	15 (3.8)	2 (0.5)	0
General physical health deterioration	19 (4.8)	12 (3.1)	2 (0.5)	3 (0.8)	15 (3.8)	7 (1.8)	1 (0.3)	2 (0.5)
Chest pain	15 (3.8)	1 (0.3)	0	0	18 (4.5)	2 (0.5)	0	0
Malaise	13 (3.3)	4 (1.0)	0	0	3 (0.8)	0	0	0
Mucosal inflammation	10 (2.5)	1 (0.3)	0	0	3 (0.8)	0	0	0
Gait disturbance	7 (1.8)	2 (0.5)	1 (0.3)	0	3 (0.8)	0	0	0
Performance status decreased	6 (1.5)	2 (0.5)	0	0	5 (1.3)	3 (0.8)	0	0
Spinal pain	6 (1.5)	2 (0.5)	0	0	10 (2.5)	2 (0.5)	0	0
Death	2 (0.5)	0	0	2 (0.5)	1 (0.3)	0	0	1 (0.3)
Multi-organ failure	2 (0.5)	0	0	2 (0.5)	4 (1.0)	0	0	4 (1.0)
Suprapubic pain	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Skin and subcutaneous tissue disorders	189 (48.1)	6 (1.5)	0	0	72 (18.2)	0	0	0
Pruritus	99 (25.2)	1 (0.3)	0	0	22 (5.6)	0	0	0
Rash	83 (21.1)	2 (0.5)	0	0	27 (6.8)	0	0	0
Urticaria	10 (2.5)	1 (0.3)	0	0	1 (0.3)	0	0	0
Erythema	9 (2.3)	1 (0.3)	0	0	1 (0.3)	0	0	0
Rash generalized	5 (1.3)	1 (0.3)	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	176 (44.8)	41 (10.4)	0	0	213 (53.8)	55 (13.9)	3 (0.8)	0
Back pain	59 (15.0)	14 (3.6)	0	0	77 (19.4)	17 (4.3)	3 (0.8)	0
Arthralgia	44 (11.2)	6 (1.5)	0	0	58 (14.6)	7 (1.8)	0	0
Bone pain	34 (8.7)	9 (2.3)	0	0	55 (13.9)	13 (3.3)	0	0
Musculoskeletal pain	32 (8.1)	1 (0.3)	0	0	47 (11.9)	9 (2.3)	0	0
Pain in extremity	32 (8.1)	4 (1.0)	0	0	43 (10.9)	9 (2.3)	0	0

Muscular weakness	18 (4.6)	8 (2.0)	0	0	16 (4.0)	4 (1.0)	0	0
Myalgia	14 (3.6)	3 (0.8)	0	0	17 (4.3)	1 (0.3)	0	0
Neck pain	13 (3.3)	0	0	0	10 (2.5)	2 (0.5)	0	0
Groin pain	7 (1.8)	0	0	0	5 (1.3)	2 (0.5)	0	0
Musculoskeletal chest pain	5 (1.3)	2 (0.5)	0	0	19 (4.8)	2 (0.5)	0	0
Flank pain	3 (0.8)	1 (0.3)	0	0	6 (1.5)	2 (0.5)	0	0
Osteonecrosis	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Myopathy	1 (0.3)	0	0	0	1 (0.3)	1 (0.3)	0	0
Metabolism and nutrition disorders	171 (43.5)	49 (12.5)	5 (1.3)	1 (0.3)	133 (33.6)	29 (7.3)	2 (0.5)	1 (0.3)
Decreased appetite	120 (30.5)	15 (3.8)	0	0	98 (24.7)	12 (3.0)	0	0
Dehydration	38 (9.7)	21 (5.3)	0	0	24 (6.1)	8 (2.0)	1 (0.3)	1 (0.3)
Hypokalemia	22 (5.6)	10 (2.5)	1 (0.3)	0	10 (2.5)	4 (1.0)	0	0
Hypocalcemia	14 (3.6)	2 (0.5)	2 (0.5)	0	7 (1.8)	1 (0.3)	0	0
Hyponatremia	13 (3.3)	7 (1.8)	0	0	4 (1.0)	2 (0.5)	0	0
Hyperglycemia	10 (2.5)	4 (1.0)	0	0	5 (1.3)	1 (0.3)	1 (0.3)	0
Hypoalbuminemia	7 (1.8)	1 (0.3)	0	0	2 (0.5)	0	0	0
Hyperuricemia	3 (0.8)	0	2 (0.5)	0	2 (0.5)	0	0	0
Failure to thrive	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Hyperkalemia	2 (0.5)	0	0	0	3 (0.8)	2 (0.5)	0	0
Acidosis	1 (0.3)	1 (0.3)	0	0	1 (0.3)	1 (0.3)	0	0
Cachexia	1 (0.3)	1 (0.3)	0	0	2 (0.5)	1 (0.3)	0	0
Diabetes mellitus	1 (0.3)	1 (0.3)	0	0	1 (0.3)	0	0	0
Hypophosphatemia	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Tumor lysis syndrome	1 (0.3)	0	0	1 (0.3)	0	0	0	0
Investigations	166 (42.2)	53 (13.5)	6 (1.5)	0	112 (28.3)	29 (7.3)	6 (1.5)	0
Weight decreased	90 (22.9)	5 (1.3)	0	0	56 (14.1)	1 (0.3)	0	0
Aspartate aminotransferase increased	36 (9.2)	12 (3.1)	2 (0.5)	0	21 (5.3)	6 (1.5)	1 (0.3)	0
Hemoglobin decreased	34 (8.7)	10 (2.5)	3 (0.8)	0	23 (5.8)	8 (2.0)	1 (0.3)	0
Alanine aminotransferase increased	29 (7.4)	9 (2.3)	0	0	9 (2.3)	3 (0.8)	0	0
Blood creatinine increased	15 (3.8)	5 (1.3)	0	0	10 (2.5)	1 (0.3)	0	0
Blood alkaline phosphatase increased	14 (3.6)	7 (1.8)	0	0	12 (3.0)	4 (1.0)	1 (0.3)	0
Blood albumin decreased	8 (2.0)	1 (0.3)	0	0	2 (0.5)	0	0	0
Platelet count decreased	8 (2.0)	3 (0.8)	0	0	5 (1.3)	1 (0.3)	1 (0.3)	0

Blood bilirubin increased	6 (1.5)	4 (1.0)	0	0	1 (0.3)	0	0	0
Blood lactate dehydrogenase increased	6 (1.5)	1 (0.3)	0	0	6 (1.5)	0	0	0
Blood potassium decreased	6 (1.5)	1 (0.3)	0	0	0	0	0	0
Blood phosphorous decreased	5 (1.3)	2 (0.5)	0	0	3 (0.8)	1 (0.3)	0	0
Liver function test abnormal	5 (1.3)	4 (1.0)	0	0	1 (0.3)	1 (0.3)	0	0
Blood sodium decreased	4 (1.0)	1 (0.3)	0	0	1 (0.3)	1 (0.3)	0	0
Blood calcium decreased	3 (0.8)	2 (0.5)	0	0	4 (1.0)	0	0	0
Blood glucose increased	3 (0.8)	1(0.3)	0	0	2 (0.5)	1 (0.3)	0	0
C-reactive protein increased	3 (0.8)	1(0.3)	0	0	0	0	0	0
Gamma-glutamyltransferase increased	3 (0.8)	1(0.3)	0	0	1 (0.3)	0	0	0
Lipase increased	3 (0.8)	0	1 (0.3)	0	3 (0.8)	2 (0.5)	0	0
Red blood cell count decreased	3 (0.8)	0	0	0	1 (0.3)	1 (0.3)	0	0
Amylase increased	2 (0.5)	2 (0.5)	0	0	1 (0.3)	0	0	0
Blood corticotrophin decreased	2 (0.5)	1 (0.3)	0	0	2 (0.5)	0	0	0
Blood creatine phosphokinase decreased	1 (0.3)	1 (0.3)	0	0	0	0	0	0
International normalized ratio increased	1 (0.3)	1 (0.3)	0	0	2 (0.5)	1 (0.3)	0	0
Thyroid function test abnormal	1 (0.3)	1 (0.3)	0	0	0	0	0	0
White blood cell count decreased	1 (0.3)	0	0	0	1 (0.3)	1 (0.3)	0	0
General physical condition abnormal	1 (0.3)	0	0	0	3 (0.8)	2 (0.5)	0	0
ECOG performance status worsened	0	0	0	0	2 (0.5)	1 (0.3)	1 (0.3)	0
Neutrophil count decreased	0	0	0	0	2 (0.5)	0	1 (0.3)	0
Heart rate irregular	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Nervous system disorders	128 (32.6)	19 (4.8)	7 (1.8)	1 (0.3)	126 (31.8)	26 (6.6)	5 (1.3)	3 (0.8)
Headache	39 (9.9)	2 (0.5)	0	0	32 (8.1)	2 (0.5)	0	0
Dizziness	23 (5.9)	1 (0.3)	0	0	18 (4.5)	1 (0.3)	0	0
Paraesthesia	11 (2.8)	1 (0.3)	0	0	10 (2.5)	1 (0.3)	0	0
Somnolence	11 (2.8)	1 (0.3)	0	0	5 (1.3)	2 (0.5)	0	0
Syncope	7 (1.8)	4 (1.0)	0	0	3 (0.8)	3 (0.8)	0	0
Peripheral motor neuropathy	6 (1.5)	3 (0.8)	0	0	4 (1.0)	3 (0.8)	0	0
Spinal cord compression	5 (1.3)	3 (0.8)	1 (0.3)	0	4 (1.0)	3 (0.8)	0	0
Peripheral neuropathy	5 (1.3)	0	0	0	8 (2.0)	1 (0.3)	0	0
Lethargy	4 (1.0)	2 (0.5)	0	0	5 (1.3)	2 (0.5)	0	0
Cerebrovascular accident	3 (0.8)	0	2 (0.5)	1 (0.3)	2 (0.5)	0	1 (0.3)	0

Cognitive disorder	3 (0.8)	2 (0.5)	0	0	1 (0.3)	0	0	0
Intracranial/cerebral hemorrhage	2 (0.5)	0	2 (0.5)	0	1 (0.3)	1 (0.3)	0	0
Presyncope	2 (0.5)	1 (0.3)	0	0	1 (0.3)	1 (0.3)	0	0
Convulsion	2 (0.5)	0	0	0	2 (0.5)	1 (0.3)	0	0
Cerebral ischemia	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Motor dysfunction	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Neuritis	1 (0.3)	0	1 (0.3)	0	0	0	0	0
Paraparesis	1 (0.3)	0	1 (0.3)	0	2 (0.5)	1 (0.3)	0	0
Paresis	1 (0.3)	0	0	0	4 (1.0)	2 (0.5)	0	0
Speech disorder	1 (0.3)	0	0	0	2 (0.5)	1 (0.3)	0	0
CNS hemorrhage	0	0	0	0	2 (0.5)	0	0	2 (0.5)
Cerebral infarction	0	0	0	0	2 (0.5)	1 (0.3)	0	0
Ataxia	0	0	0	0	2 (0.5)	1 (0.3)	0	0
Cerebrovascular disorder	0	0	0	0	1 (0.3)	0	0	1 (0.3)
Brachial plexopathy	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Neurological symptom	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Paraplegia	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Subarachinoid hemorrhage	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Transient ischemic attack	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Trigeminal nerve disorder	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Loss of consciousness	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Infections and infestations	123 (31.3)	36 (9.2)	4 (1.0)	7 (1.8)	94 (23.7)	14 (3.5)	6 (1.5)	2 (0.5)
Urinary tract infection	31 (7.9)	12 (3.1)	1 (0.3)	0	27 (6.8)	4 (1.0)	0	0
Pneumonia	24 (6.1)	11 (2.8)	1 (0.3)	4 (1.0)	9 (2.3)	2 (0.5)	1 (0.3)	0
Infection	8 (2.0)	3 (0.8)	0	0	8 (2.0)	3 (0.8)	0	0
Oral candidiasis	8 (2.0)	1 (0.3)	0	0	3 (0.8)	0	0	0
Cystitis	6 (1.5)	0	1 (0.3)	0	3 (0.8)	1 (0.3)	0	0
Herpes zoster	6 (1.5)	1 (0.3)	0	0	2 (0.5)	1 (0.3)	0	0
Sepsis	5 (1.3)	3 (0.8)	0	2 (0.5)	3 (0.8)	1 (0.3)	1 (0.3)	1 (0.3)
Cellulitis	3 (0.8)	0	0	1 (0.3)	3 (0.8)	1 (0.3)	1 (0.3)	0
Lower respiratory tract infection	3 (0.8)	1 (0.3)	0	0	3 (0.8)	0	0	0
Respiratory tract infection	3 (0.8)	2 (0.5)	0	0	3 (0.8)	2 (0.5)	0	0
Device-related infection	2 (0.5)	1 (0.3)	0	0	0	0	0	0

Gastroenteritis	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Gastroenteritis viral	0	0	0	0	1 (0.3)	0	0	0
Subcutaneous abscess	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Clostridium difficile colitis	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Epstein-Barr virus infection	1 (0.3)	0	1 (0.3)	0	0	0	0	0
Lung infection	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Periorbital cellulitis	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Peritonitis	1 (0.3)	0	1 (0.3)	0	0	0	0	0
Septic shock	1 (0.3)	0	0	1 (0.3)	0	0	0	0
Streptococcal bacteremia	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Lobar pneumonia	1 (0.3)	0	0	0	1 (0.3)	0	1 (0.3)	0
Bronchopneumonia	0	0	0	0	3 (0.8)	0	0	1 (0.3)
Cavernous sinus thrombosis	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Central nervous system infection	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Bacterial sepsis	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Enterocolitis infectious	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Myelitis	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Urosepsis	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Respiratory, thoracic, and mediastinal disorders	111 (28.2)	22 (5.6)	4 (1.0)	6 (1.5)	80 (20.2)	9 (2.3)	7 (1.8)	3 (0.8)
Dyspnea	50 (12.7)	15 (3.8)	3 (0.8)	0	36 (9.1)	5 (1.3)	2 (0.5)	0
Cough	36 (9.2)	2 (0.5)	0	0	27 (6.8)	0	0	0
Pleural effusion	11 (2.8)	2 (0.5)	0	1 (0.5)	11 (2.8)	1 (0.3)	1 (0.3)	0
Oropharyngeal pain	7 (1.8)	1 (0.3)	0	0	3 (0.8)	0	0	0
Pneumonitis	5 (1.3)	1 (0.3)	0	0	0	0	0	0
Pulmonary embolism	4 (1.0)	1 (0.3)	1 (0.3)	1 (0.3)	5 (1.3)	0	2 (0.5)	2 (0.5)
Epistaxis	4 (1.0)	0	0	0	2 (0.5)	1 (0.3)	0	0
Bronchospasm	3 (0.8)	1 (0.3)	0	0	1 (0.3)	1 (0.3)	0	0
Hypoxia	3 (0.8)	2 (0.5)	0	0	2 (0.5)	2 (0.5)	0	0
Pneumonia aspiration	3 (0.8)	0	0	2 (0.5)	1 (0.3)	0	1 (0.3)	0
Acute pulmonary edema	2 (0.5)	1 (0.3)	0	1 (0.3)	1 (0.3)	0	1 (0.3)	0
Apnea	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Aspiration	1 (0.3)	1 (0.3)	0	0	0	0	0	0

Pulmonary edema	1 (0.3)	0	0	1 (0.3)	0	0	0	0
Acute respiratory failure	0	0	0	0	1 (0.3)	0	0	1 (0.3)
Respiratory failure	0	0	0	0	1 (0.3)	0	0	1 (0.3)
Hiccups	0	0	0	0	2 (0.5)	1 (0.3)	0	0
Lung disorder	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Pulmonary hypertension	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Blood and lymphatic system disorders	102 (26.0)	39 (9.9)	5 (1.3)	0	103 (26.0)	38 (9.6)	14 (3.5)	0
Anemia	90 (22.9)	37 (9.4)	3 (0.8)	0	88 (22.2)	35 (8.8)	8 (2.0)	0
Thrombocytopenia	9 (2.3)	2 (0.5)	1 (0.3)	0	18 (4.5)	3 (0.8)	5 (1.3)	0
Neutropenia	7 (1.8)	0	0	0	8 (2.0)	3 (0.8)	0	0
Febrile neutropenia	2 (0.5)	1 (0.3)	1 (0.3)	0	1 (0.3)	0	1 (0.3)	0
Lymphadenopathy	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Coagulopathy	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Hemolysis	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Leukopenia	1 (0.3)	1 (0.3)	0	0	7 (1.8)	2 (0.5)	1 (0.3)	0
Lymphopenia	1 (0.3)	0	0	0	4 (1.0)	1 (0.3)	1 (0.3)	0
Renal and urinary disorders	74 (18.8)	21 (5.3)	2 (0.5)	2 (0.5)	60 (15.2)	20 (5.1)	1 (0.3)	0
Hematuria	15 (3.8)	2 (0.5)	0	0	15 (3.8)	4 (1.0)	0	0
Urinary retention	12 (3.1)	2 (0.5)	0	0	10 (2.5)	2 (0.5)	0	0
Urinary incontinence	10 (2.5)	2 (0.5)	0	0	4 (1.0)	2 (0.5)	0	0
Acute renal failure	9 (2.3)	6 (1.5)	1 (0.3)	1 (0.3)	2 (0.5)	2 (0.5)	0	0
Dysuria	8 (2.0)	0	0	0	6 (1.5)	1 (0.3)	0	0
Proteinuria	6 (1.5)	0	0	0	6 (1.5)	1 (0.3)	0	0
Renal failure	6 (1.5)	3 (0.8)	1 (0.3)	1 (0.3)	4 (1.0)	3 (0.8)	0	0
Nocturia	3 (0.8)	1 (0.3)	0	0	3 (0.8)	0	0	0
Ureteric obstruction	3 (0.8)	3 (0.8)	0	0	0	0	0	0
Urethral obstruction	0	0	0	0	1 (0.3)	0	0	0
Bladder obstruction	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Hydronephrosis	2 (0.5)	1 (0.3)	0	0	5 (1.3)	2 (0.5)	1 (0.3)	0
Micturition urgency	2 (0.5)	1 (0.3)	0	0	2 (0.5)	1 (0.3)	0	0
Renal impairment	2 (0.5)	0	0	0	2 (0.5)	1 (0.3)	0	0
Bladder dilatation	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Pyelocaliectasis	1 (0.3)	1 (0.3)	0	0	0	0	0	0

Renal injury	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Anuria	1 (0.3)	0	0	0	1 (0.3)	1 (0.3)	0	0
Psychiatric disorders	73 (18.6)	10 (2.5)	3 (0.8)	1 (0.3)	74 (18.7)	11 (2.8)	1 (0.3)	0
Insomnia	31 (7.9)	0	0	0	34 (8.6)	3 (0.8)	0	0
Confusional state	14 (3.6)	3 (0.8)	1 (0.3)	0	12 (3.0)	4 (1.0)	0	0
Depression	11 (2.8)	3 (0.8)	1 (0.3)	0	20 (5.1)	1 (0.3)	0	0
Hallucination	4 (1.0)	2 (0.5)	0	0	1 (0.3)	1 (0.3)	0	0
Agitation	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Delirium	2 (0.5)	1 (0.3)	0	0	1 (0.3)	1 (0.3)	0	0
Restlessness	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Self injurious behavior	1 (0.3)	0	0	1 (0.3)	0	0	0	0
Suicidal ideation	1 (0.3)	0	1 (0.3)	0	0	0	0	0
Major depression	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Hallucination, visual	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Vascular disorders	64 (16.3)	10 (2.5)	0	0	50 (12.6)	7 (1.8)	0	1 (0.3)
Hypertension	20 (5.1)	1 (0.3)	0	0	13 (3.3)	1 (0.3)	0	0
Hypotension	19 (4.8)	4 (1.0)	0	0	14 (3.5)	1 (0.3)	0	0
Hot flush	7 (1.8)	1 (0.3)	0	0	3 (0.8)	0	0	0
Deep vein thrombosis	5 (1.3)	2 (0.5)	0	0	3 (0.8)	3 (0.8)	0	0
Thrombosis	2 (0.5)	1 (0.3)	0	0	0	0	0	0
Hypovolemic shock	1 (0.3)	1 (0.3)	0	0	1 (0.3)	0	0	1 (0.3)
Venous thrombosis	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Orthostatic hypotension	0	0	0	0	2 (0.5)	1 (0.3)	0	0
Peripheral ischemia	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Neoplasms (benign, malignant, and unspecified)	46 (11.7)	6 (1.5)	5 (1.3)	32 (8.1)	46 (11.6)	6 (1.5)	5 (1.3)	24 (6.1)
Malignant neoplasm progression	36 (9.2)	3 (0.8)	2 (0.5)	30 (7.6)	31 (7.8)	2 (0.5)	3 (0.8)	24 (6.1)
Tumor pain	3 (0.8)	1 (0.3)	1 (0.3)	0	5 (1.3)	1 (0.3)	0	0
Metastases to bone	2 (0.5)	0	1 (0.3)	0	1 (0.3)	1 (0.3)	0	0
Cerebellopontine angle tumor	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Lymphangiosis carcinomatosa	1 (0.3)	0	0	1 (0.3)	0	0	0	0
Malignant neoplasm of spinal cord	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Prostate cancer	1 (0.3)	0	0	1 (0.3)	0	0	0	0

Metastatic prostate cancer	1 (0.3)	0	1 (0.3)	0	0	0	0	0
Tumor associated fever	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Metastases to central nervous system	0	0	0	0	2 (0.5)	0	1 (0.3)	0
Metastatic neoplasm	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Cancer pain	0	0	0	0	2 (0.5)	2 (0.5)	0	0
Eye disorders	37 (9.4)	2 (0.5)	1 (0.3)	0	28 (7.1)	4 (1.0)	1 (0.3)	0
Blindness	1 (0.3)	0	1 (0.3)	0	0	0	0	0
Cataract	1 (0.3)	1 (0.3)	0	0	1 (0.3)	1 (0.3)	0	0
Uveitis	1 (0.3)	1 (0.3)	0	0	1 (0.3)	0	0	0
Visual impairment	1 (0.3)	0	0	0	4 (1.0)	1 (0.3)	0	0
Papilloedema	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Retinal vein thrombosis	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Visual acuity reduced	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Cardiac disorders	35 (8.9)	9 (2.3)	3 (0.8)	9 (2.3)	27 (6.8)	2 (0.5)	1 (0.3)	5 (1.3)
Atrial fibrillation	5 (1.3)	4 (1.0)	0	1 (0.3)	4 (1.0)	0	0	0
Arrhythmia	3 (0.8)	0	1 (0.3)	0	0	0	0	0
Cardiac failure	3 (0.8)	2 (0.5)	0	1 (0.3)	2 (0.5)	0	0	1 (0.3)
Pericardial effusion	3 (0.8)	1 (0.3)	0	0	0	0	0	0
Acute myocardial infarction	2 (0.5)	0	1 (0.3)	1 (0.3)	1 (0.3)	0	0	0
Cardiac arrest	2 (0.5)	0	0	2 (0.5)	0	0	0	0
Cardio-respiratory arrest	2 (0.5)	0	0	2 (0.5)	2 (0.5)	0	0	2 (0.5)
Myocardial infarction	2 (0.5)	0	1 (0.3)	1 (0.3)	1 (0.3)	0	0	1 (0.3)
Unstable angina	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Bradycardia	1 (0.3)	1 (0.3)	0	0	1 (0.3)	0	0	0
Acute cardiac failure	1 (0.3)	0	1 (0.3)	0	0	0	0	0
Cardiopulmonary failure	1 (0.3)	0	0	1 (0.3)	1 (0.3)	0	0	1 (0.3)
Cardiac failure congestive	0	0	0	0	1 (0.3)	0	1 (0.3)	0
Cardiac valve disease	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Tachyarrhythmia	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Injury, poisoning, and procedural complications	31 (7.9)	10 (2.5)	0	0	21 (5.3)	3 (0.8)	1 (0.3)	0
Fall	7 (1.8)	1 (0.3)	0	0	3 (0.8)	0	0	0
Fracture	3 (0.8)	1 (0.3)	0	0	0	0	0	0

Subdural hematoma	2 (0.5)	2 (0.5)	0	0	2 (0.5)	1 (0.3)	1 (0.3)	0
Ankle fracture	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Bone fissure	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Femur fracture	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Hip fracture	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Humerus fracture	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Toxicity to various agents	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Eschar	1 (0.3)	0	0	0	1 (0.3)	1 (0.3)	0	0
Femoral neck fracture	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Endocrine disorders	21 (5.3)	6 (1.5)	0	0	8 (2.0)	2 (0.5)	0	0
Hypothyroidism	9 (2.3)	2 (0.5)	0	0	1 (0.3)	0	0	0
Adrenal insufficiency	6 (1.5)	2 (0.5)	0	0	3 (0.8)	1 (0.8)	0	0
Hyperthyroidism	6 (1.5)	1 (0.3)	0	0	0	0	0	0
Hypophysitis	4 (1.0)	1 (0.3)	0	0	2 (0.5)	1 (0.3)	0	0
Hypopituitarism	3 (0.8)	3 (0.8)	0	0	0	0	0	0
Hepatobiliary disorders	20 (5.1)	6 (1.5)	1 (0.3)	3 (0.8)	6 (1.5)	1 (0.3)	0	1 (0.3)
Hepatitis	5 (1.3)	1 (0.3)	0	1 (0.3)	0	0	0	0
Jaundice	5 (1.3)	1 (0.3)	0	0	0	0	0	0
Autoimmune hepatitis	3 (0.8)	2 (0.5)	0	0	0	0	0	0
Hepatotoxicity	2 (0.5)	2 (0.5)	0	0	0	0	0	0
Cholangitis	1 (0.3)	0	0	1 (0.3)	0	0	0	0
Acute cholecystitis	1 (0.3)	0	1 (0.3)	0	0	0	0	0
Chronic cholecystitis	1 (0.3)	1 (0.3)	0	0	0	0	0	0
Hepatic failure	1 (0.3)	0	0	1 (0.3)	0	0	0	0
Jaundice cholestatic	0	0	0	0	1 (0.3)	0	0	1 (0.3)
Hepatic function abnormal	0	0	0	0	1 (0.3)	1 (0.3)	0	0
Reproductive system and breast disorders	11 (2.8)	0	0	0	16 (4.0)	1 (0.3)	0	0
Pelvic pain	5 (1.3)	0	0	0	9 (2.3)	1 (0.3)	0	0
Drug-related event	295 (75.1)	123 (31.3)	19 (4.8)	3 (0.8)	180 (45.5)	33 (8.3)	7 (1.8)	1 (0.3)
Events leading to discontinuation	137 (34.9)	80 (20.4)	19 (4.8)	22 (5.6)	62 (15.7)	25 (6.3)	8 (2.0)	15 (3.8)
Immune-related events	249 (63.4)	93 (23.7)	8 (2.0)	1 (0.3)	86 (21.7)	11 (2.8)	0	1 (0.3)
Gastrointestinal**	160 (40.7)	65 (16.5)	6 (1.5)	1 (0.3)	56 (14.1)	3 (0.8)	0	0
Diarrhea	155 (39.4)	58 (14.8)	1 (0.3)	0	55 (13.9)	3 (0.8)	0	0

Colitis	27 (6.9)	15 (3.8)	3 (0.8)	0	3 (0.8)	0	0	0
Skin	137 (34.9)	4 (1.0)	0	0	29 (7.3)	0	0	0
Pruritus	80 (20.4)	1 (0.3)	0	0	15 (3.8)	0	0	0
Rash	68 (17.3)	2 (0.5)	0	0	16 (4.0)	0	0	0
Investigations	35 (8.9)	15 (3.8)	2 (0.5)	0	20 (5.1)	6 (1.5)	1 (0.3)	0
Aspartate aminotransferase increased	22 (5.6)	8 (2.0)	1 (0.3)	0	13 (3.3)	3 (0.8)	1 (1.0)	0
Alanine aminotransferase increased	20 (5.1)	6 (1.5)	0	0	8 (2.0)	3 (0.8)	0	0
Lipase increased	2 (0.5)	0	1 (0.3)	0	2 (0.5)	2 (0.5)	0	0
Endocrine	18 (4.6)	6 (1.5)	0	0	4 (1.0)	2 (0.5)	0	0
Hypothyroidism	9 (2.3)	2 (0.5)	0	0	1 (0.3)	0	0	0
Adrenal insufficiency	6 (1.5)	2 (0.5)	0	0	2 (0.5)	1 (0.3)	0	0
Hepatobiliary disorders	11 (2.8)	5 (1.3)	0	0	0	0	0	0
Hepatitis	3 (0.8)	1 (0.3)	0	0	0	0	0	0
Hepatotoxicity	2 (0.5)	2 (0.5)	0	0	0	0	0	0
Neurologic	8 (2.0)	1 (0.3)	0	0	1 (0.3)	0	0	0
Motor dysfunction	1 (0.3)	1 (0.3)	0	0	0	0	0	0

Data are n (%). Patients may have had more than one event.

*Events of any grade that occurred in ≥10% of patients in one or both treatment arms or any event of grade 3, 4, or 5 severity.

**Incidence of GI perforation was 0.5%.

Supplementary Table 5: On-study AEs by pretreatment RT to pelvis vs non-pelvis

	Pelvis RT		Non-pelvis RT	
	Ipilimumab + RT (n=141)	**Placebo + RT (n=122)**	**Ipilimumab + RT (n=252)**	**Placebo + RT (n=274)**
Any AE	139 (98.6)	112 (91.8)	246 (97.6)	252 (92.0)
Grade 3 or 4	78 (55.3)	57 (46.7)	154 (61.1)	105 (38.3)
Fatal AE	28 (19.9)	10 (8.2)	38 (15.1)	6 (2.2)
GI AEs, any grade	109 (77.3)	76 (62.3)	176 (69.8)	148 (54.0)
Grade 3 or 4	36 (25.5)	13 (10.7)	55 (21.8)	20 (7.3)
Diarrhea, any grade	79 (56.0)	32 (26.2)	120 (47.6)	65 (23.7)
Grade 3 or 4	28 (19.9)	3 (2.5)	36 (14.3)	4 (1.5)

Supplementary Table 6: Time to onset and resolution of grade 3 or 4 immune-related adverse events for ipilimumab-treated patients

Organ system	Time to onset		Time to resolution	
	No. events treated*	Median (weeks, 95% CI)	No. events resolved (%)**	Median (weeks, 95% CI)
Gastrointestinal	71	5.7 (4.9–7.0)	63 (89)	2.9 (1.6–4.7)
Hepatic	18	9.1 (8.3–10.4)	18 (100)	4.1 (3.6–8.1)
Endocrine	8	7.9 (4.1–11.1)	6 (75)	11.1 (2.4–NE)
Skin	4	3.7 (2.6–6.4)	4 (100)	3.6 (2.6–5.9)
Neurological	1	11.1 (NE)	0 (0)	---

*No. of events equal to number of patients; one event occurred per patient.

**Resolution of a grade 3 or 4 immune-related adverse event was defined as improvement to grade 1 or less or to the worst grade at baseline.

NE=not estimable due to censored observations or median not having been observed.

Supplementary Table 7: Deaths among treated patients

	Ipilimumab (n=393)	**Placebo (n=396)**
Total deaths	266 (68%)	304 (77%)
Disease progression	204 (52%)	243 (61%)
Study drug toxic effects	4 (1%)	0
Other*	47 (12%)	38 (10%)
Unknown	11 (3%)	23 (6%)

Data are n (%). *Two additional patients in the ipilimumab group and one in the placebo group died of drug-related serious adverse events.

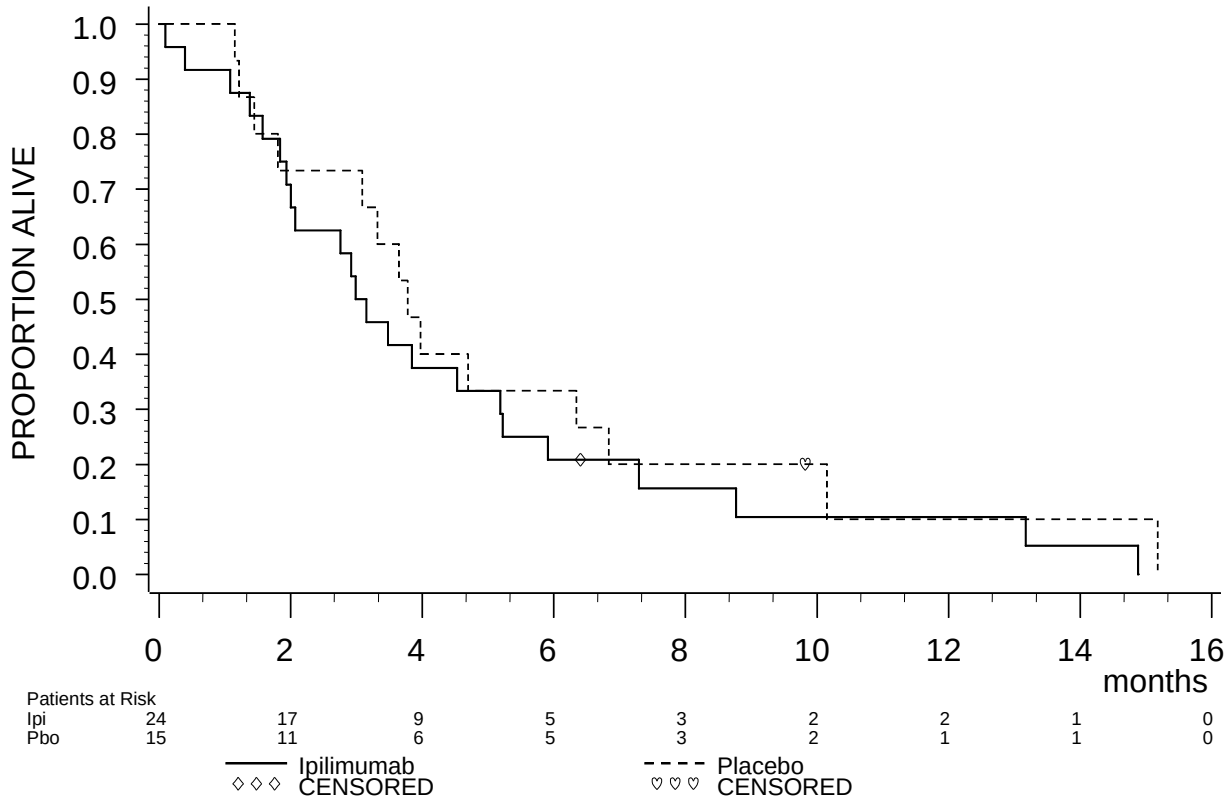
Supplementary Table 8: Baseline prognostic factors for patients who lived ≤5 months and for those who lived >5 months

	OS ≤5 months		OS >5 months	
	Ipilimumab	**Placebo**	**Ipilimumab**	**Placebo**
Number of patients	117	90	282	310
Hemoglobin <11 g/dL (per IVRS and CRF), %	38.5	32.2	18.4	20
Hemoglobin <11 g/dL (CRF), %	44.4	38.9	22.7	24.5
ECOG 0 (per IVRS and CRF), %	30.8	25.6	41.5	39.7
ECOG 1 (per IVRS and CRF), %	65	58.9	45.4	48
ECOG 0 (CRF), %	31.6	34.4	46.5	44.8
ECOG 1 (CRF), %	65	58.9	49.6	53.9
ALP ≥1.5 x ULN (IVRS and CRF), %	54.7	51.1	27	27.7
ALP ≥1.5 x ULN (CRF), %	63.2	58.9	31.6	31.6
Age ≥70	53.8	45.6	42.9	40.3
Liver metastases, %	23.1	22.2	7.8	8.7
Visceral metastases, %	43.6	44.4	22	23.9
PSA, median	270	292.5	110	118
Elevated baseline LDH, %	29.9	34.4	8.2	7.1
Average daily worst pain intensity ≥4, %	60.7	53.3	44.7	44.5

CRF=case report form. IVRS=Interactive Voice Response System.

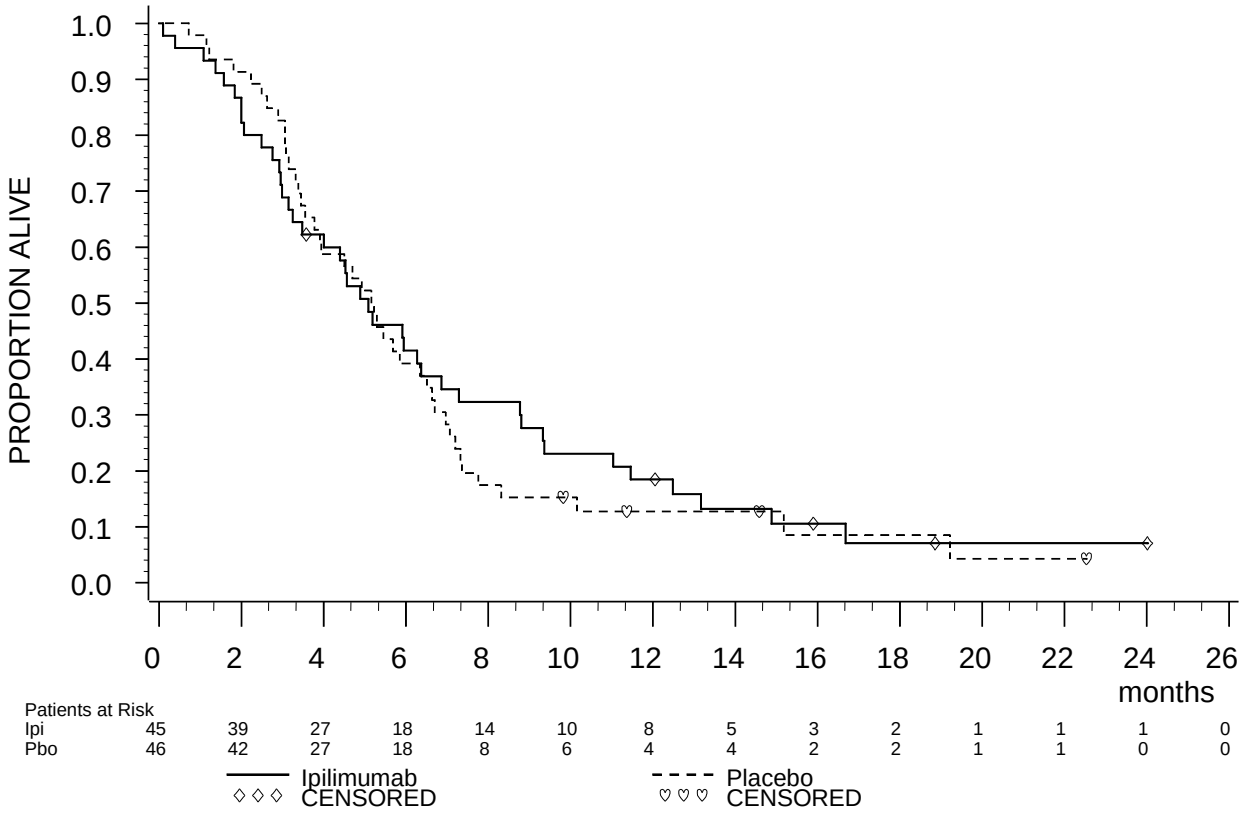
Supplementary Figure 1: Multivariate analyses of baseline prognostic features

Subgroup analysis of OS in patients with alkaline phosphatase ≥1.5 x ULN, hemoglobin <11 g/dL, and presence of visceral metastases (ipilimumab, n=24; placebo, n=15).



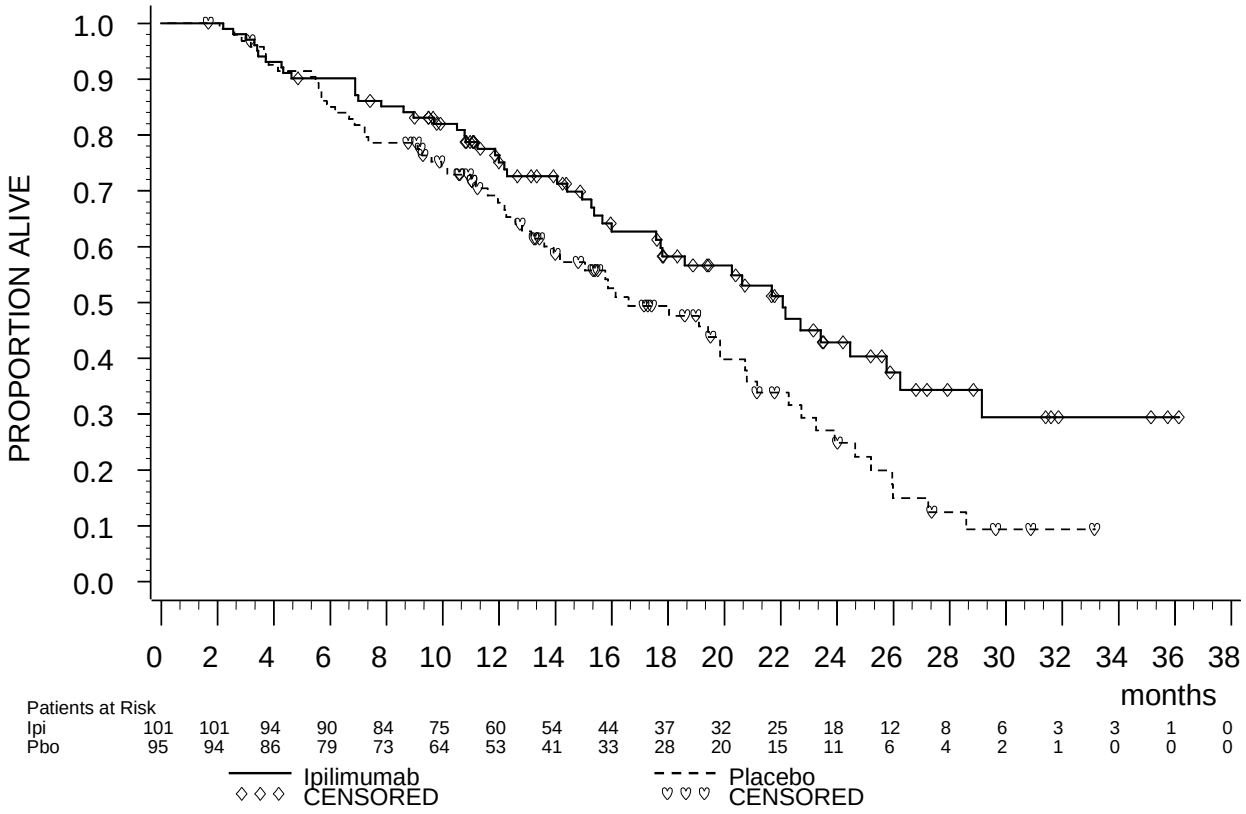
GROUP	# DEAD / # RANDOMIZED	MEDIAN (95% CI)	HAZARD RATIO (95% CI)
Ipilimumab	23/24	3.1 (2.0 - 5.2)	
Placebo	14/15	3.8 (3.1 - 6.3)	
Ipilimumab over Placebo			1.32 (0.67 - 2.62)

Subgroup analysis of OS in patients with alkaline phosphatase ≥1.5 x ULN, hemoglobin <11 g/dL, and an ECOG performance status of 1 (ipilimumab, n=45; placebo, n=46).



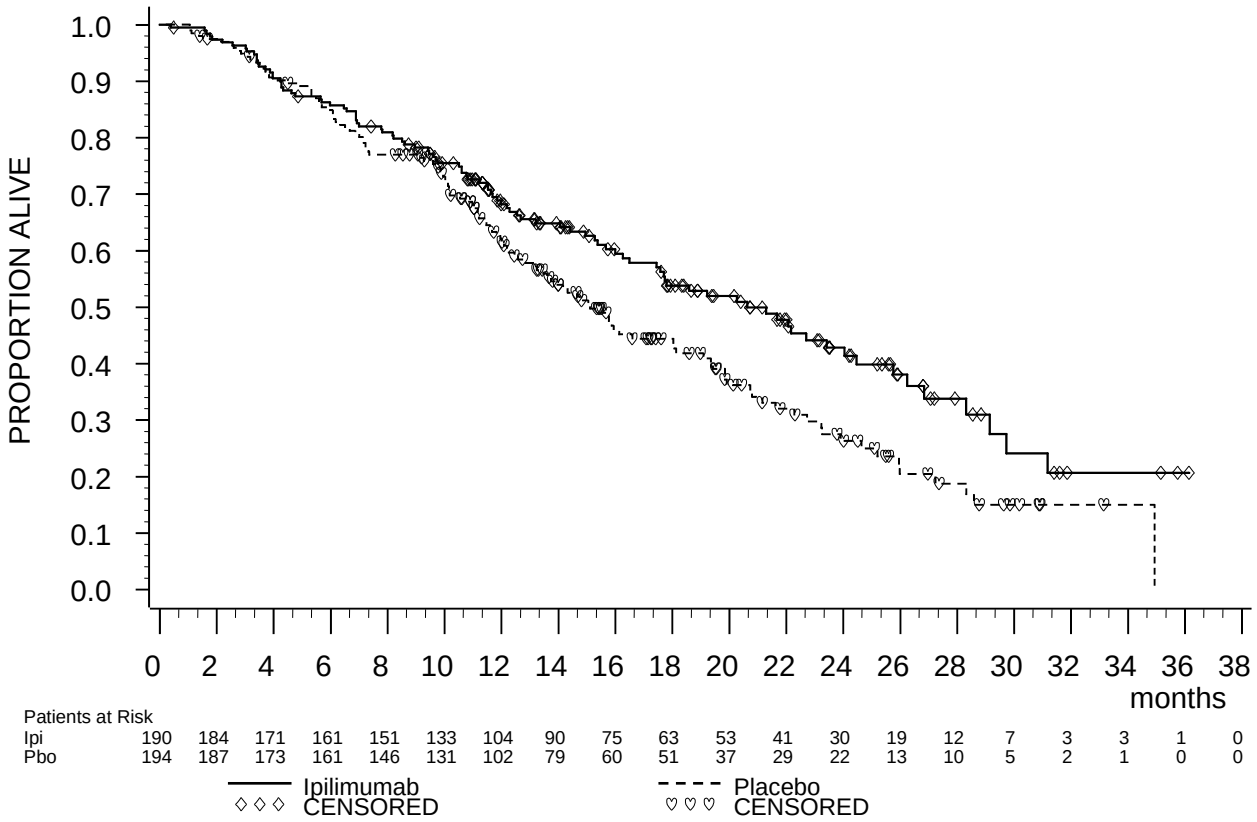
GROUP	# DEAD / # RANDOMIZED	MEDIAN (95% CI)	HAZARD RATIO (95% CI)
Ipilimumab	40/45	5.1 (3.5 - 6.9)	
Placebo	42/46	5.2 (3.8 - 6.5)	
Ipilimumab over Placebo			0.91 (0.59 - 1.41)

Subgroup analysis of OS in patients with alkaline phosphatase <1.5 x ULN, hemoglobin ≥11 g/dL, and an ECOG performance status of 0 (ipilimumab, n=101; placebo, n=95).



GROUP	# DEAD / # RANDOMIZED	MEDIAN (95% CI)	HAZARD RATIO (95% CI)
Ipilimumab	48/101	22.1 (17.7 - 26.3)	
Placebo	60/95	16.6 (13.6 - 20.7)	
Ipilimumab over Placebo			0.63 (0.43 - 0.92)

Subgroup analysis of OS in patients with alkaline phosphatase <1.5 x ULN and hemoglobin ≥11 g/dL (ipilimumab, n=190; placebo, n=194).



GROUP	# DEAD / # RANDOMIZED	MEDIAN (95% CI)	HAZARD RATIO (95% CI)
Ipilimumab	96/190	20.6 (17.4 - 24.5)	
Placebo	122/194	15.1 (13.1 - 18.1)	
Ipilimumab over Placebo			0.71 (0.54 - 0.93)

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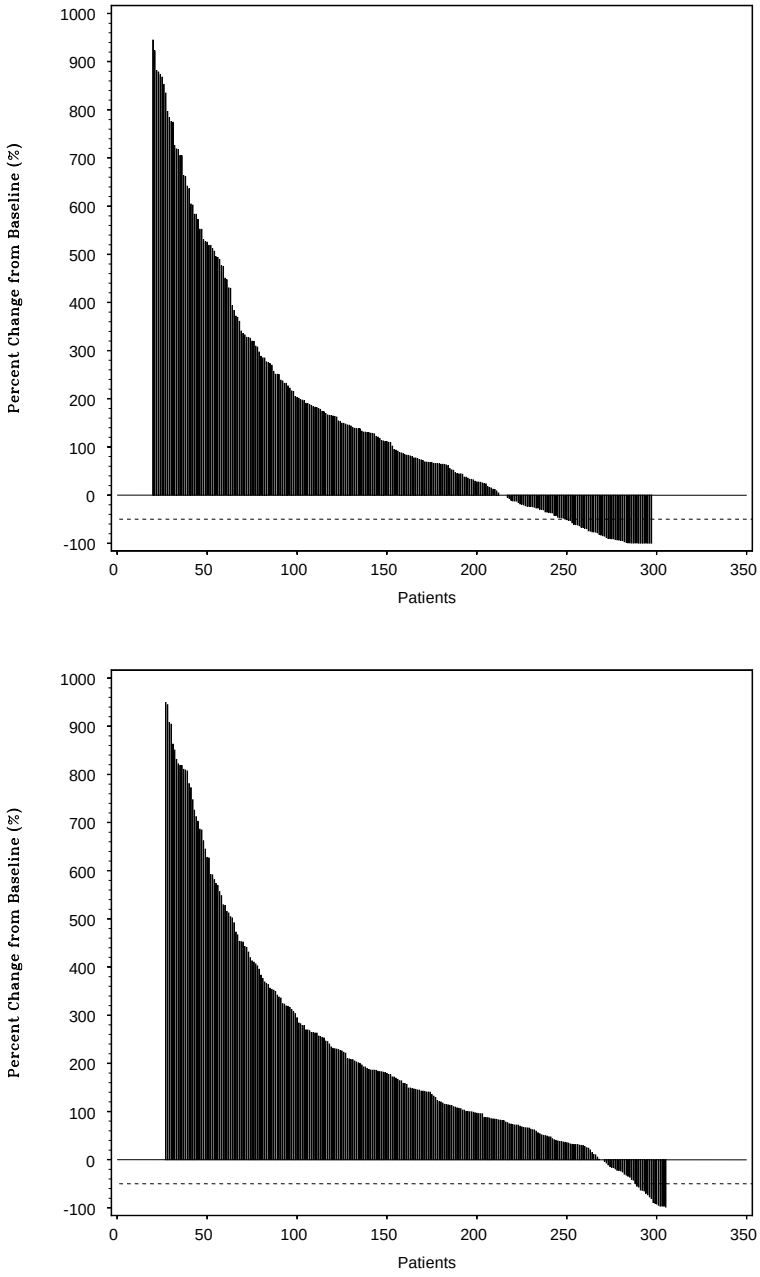
Supplementary Figure 2: Waterfall plots of PSA levels

Maximum percent change in PSA levels from baseline in the ipilimumab arm (n=297; top panel) and in the placebo arm (n=305; bottom panel).



Investigator list

Country	Investigator	Site #	Subjects Enrolled	Subjects Treated
USA	Eugene D. Kwon	00025	41	37
France	Alberto Bossi	00116	30	29
Netherlands	Alfons Van Den Eertwegh	00006	29	26
France	Guilhem Roubaud	00115	18	15
Austria	Michael Krainer	00004	17	17
Australia	Siobhan Ng	00055	17	13
Mexico	Samuel Rivera	00078	15	10
Denmark	Lisa Sengelov	00087	15	11
Brazil	Carlos Dzik	00104	15	8
Brazil	Fabio Andre Franke	00105	15	13
USA	Neeraj Agarwal	00155	15	13
France	Hakim Mahammedi	00156	15	14
United Kingdom	Santhanam Sundar	00145	14	12
Italy	Michele Maio	00061	13	13
Denmark	Steinbjorn Hansen	00089	13	11
Netherlands	Andre M Bergman	00167	13	12
Italy	Paolo Ascierto	00062	12	8
Argentina	Ricardo Santos	00094	12	10
Spain	Joan Carles	00169	12	10
Romania	Ciuleanu Tudor Eliade	00187	12	12
Argentina	Ernesto Korbenfeld	00221	12	12
Belgium	Thierry Gil	00008	11	10
Mexico	Pedro Solano	00044	11	10
USA	Nashat Y Gabrail	00146	11	8
Italy	Ruggero Ridolfi	00191	11	10
Spain	SUSAna Hernando	00238	11	9
Brazil	Markus Gifoni	00066	10	6
Peru	Alejandro Figueroa	00084	10	8
Czech Republic	Jana Katolicka	00166	10	9
United Kingdom	Sanjay Dixit	00181	10	8
Chile	Francisco Orlandi	00230	10	7
Germany	Jochen Gleissner	00001	9	8
USA	Peter J Van Veldhuizen	00037	9	6
Russian Federation	Vsevolod Matveev	00072	9	6
Hungary	Istvan Bodrogi	00133	9	9
Chile	Eduardo Yanez	00147	9	9

Country	Investigator	Site #	Subjects Enrolled	Subjects Treated
USA	Russell Szmulewitz	00034	8	6
USA	James Wade	00040	8	7
Germany	Frank Lohr	00059	8	7
Italy	Eugenio Villa	00064	8	8
Brazil	Johnny Camargo	00070	8	7
Denmark	Lise Bentzen	00074	8	6
Argentina	Luis Enrique Fein	00096	8	6
USA	Scott T Tagawa	00178	8	7
USA	Chien-Shing Chen	00183	8	6
Germany	Sebastian Rogenhofer	00199	8	7
Argentina	Juan Ignacio Hernandez Moran	00220	8	7
Argentina	Luis Alberto Kaen	00229	8	7
Australia	Vinod Ganju	00052	7	6
Australia	Phillip Parente	00053	7	4
Brazil	Felipe Cruz	00069	7	5
USA	Manuel R Modiano	00086	7	4
Chile	Hans Harbst	00113	7	7
Spain	Rafael Lopez	00118	7	2
Russian Federation	Oleg Karyakin	00206	7	6
Brazil	Daniel Grabarz	00217	7	6
France	Antoine Thiery-Vuillemin	00226	7	5
USA	Julio J Hajdenberg	00012	6	4
Italy	Alessandro Bertolini	00063	6	3
Brazil	Alessandra Notari	00065	6	3
Brazil	Carlos Henrique Barrios	00067	6	3
Russian Federation	Mikhail Biakhov	00073	6	4
Russian Federation	Alexander Nosov	00101	6	4
USA	Ari Baron	00119	6	5
Spain	Enrique Gallardo	00121	6	4
Romania	Doina Elena Ganea	00130	6	5
Romania	Bacanu Florin	00132	6	6
Brazil	Angelica Nogueira Rodrigues	00143	6	2
Mexico	Henry Duran	00198	6	4
Chile	Pablo Gonzalez Mella	00215	6	4
USA	Laurent Gressot	00264	6	5
Belgium	Denis Schallier	00019	5	2

Country	Investigator	Site #	Subjects Enrolled	Subjects Treated
USA	Hassan H Ghazal	00038	5	5
USA	Padmanee Sharma	00071	5	5
Mexico	Hector Gonzalez	00080	5	5
Denmark	Gedske Daugaard	00088	5	4
Czech Republic	Jiri Petera	00102	5	5
Denmark	Mats Holmberg	00110	5	4
USA	Mohamad Khasawneh	00126	5	5
Hungary	Bela Piko	00134	5	4
USA	Charles Drake	00159	5	4
USA	Viran Roger Holden	00209	5	4
Argentina	Felipe Salvador Palazzo	00246	5	3
USA	Troy Guthrie Jr.	00010	4	3
USA	William R Clark	00047	4	2
Puerto Rico	Hector Velez	00077	4	3
Mexico	Jose Manuel Tello	00079	4	3
Argentina	Marcelo Tatangelo	00090	4	2
Argentina	Carlos Medina	00112	4	2
Ireland	Ray Mcdermott	00161	4	2
Canada	Fred Saad	00190	4	3
Mexico	German Castelazo Rico	00193	4	3
Argentina	Monica Rondinon	00210	4	4
France	Marjorie Baciuchka-Palmaro	00225	4	3
Greece	Eleni Efstathiou	00245	4	1
Colombia	Manuel Gonzalez	00269	4	3
Hungary	Zoltan Volgyi	00272	4	4
Spain	Jose Cervera Grau	00276	4	3
Austria	Felix Sedlmayer	00003	3	2
USA	Christopher Hagenstad	00024	3	2
USA	Alexander Hantel	00036	3	3
USA	Fadi Estephan	00048	3	2
Canada	Catherine Sperlich	00056	3	3
Argentina	Eduardo Richardet	00091	3	2
Hungary	Gabor Pajkos	00135	3	2
USA	Daniel Vaena	00136	3	3
USA	Jeffrey George	00140	3	2
Ireland	John A Mccaffrey	00168	3	2
Colombia	Ricardo Schlesinger	00184	3	3
Germany	Frank Koenig	00192	3	2
Peru	Claudia Lozada	00218	3	3

Country	Investigator	Site #	Subjects Enrolled	Subjects Treated
United Kingdom	Saad Tahir	00219	3	2
USA	Murthy V.S Andavolu	00240	3	2
France	Pascal Blanchet	00242	3	3
Peru	Jorge Becerra Giraldez	00244	3	2
Israel	Eliahu Gez	00253	3	2
Israel	Raanan Berger	00254	3	3
USA	Brendan Curti	00011	2	2
Belgium	Jean-Pascal Machiels	00021	2	2
USA	Ray D Page	00030	2	2
USA	Sanjiv S. Agarwala	00046	2	1
USA	Stephen P Kahanic	00051	2	2
Germany	Peter Staib	00058	2	1
USA	Mary-Ellen Taplin	00099	2	2
USA	Raymond J Vivacqua	00103	2	1
Spain	Miguel Climent	00117	2	2
USA	Andrew Liman	00129	2	1
United Kingdom	Ananya Choudhury	00144	2	2
Poland	Sergiusz Nawrocki	00162	2	0
USA	Ali R Golshayan	00170	2	2
USA	Tanya Dorff	00172	2	2
United Kingdom	John Staffurth	00173	2	2
USA	William R Berry	00189	2	1
Italy	Ruggero Ridolfi	00196	2	2
USA	Leslie Oleksowicz	00200	2	2
Australia	Arun Azad	00201	2	2
USA	Mark Scholz	00207	2	2
USA	John Migas	00211	2	0
Argentina	Emilio Batagelj	00216	2	2
Israel	Avivit Peer	00251	2	2
Argentina	Norma Pilnik	00273	2	2
USA	Barry C Mirtsching	00018	1	1
Belgium	Filip Van Aelst	00020	1	1
USA	Marsha Fink	00045	1	1
USA	SUSAn F Slovin	00049	1	1
Peru	Milagros Cavero	00085	1	1
Argentina	Gonzalo Giornelli	00093	1	1
Peru	Milagros Huaringa	00097	1	1
Russian Federation	Sergey Ivanov	00100	1	1
USA	Joseph Beck	00142	1	0

Country	Investigator	Site #	Subjects Enrolled	Subjects Treated
Brazil	Marcelo Oliveira	00153	1	1
Ireland	John A Mccaffrey	00160	1	0
USA	Gregory A Daniels	00202	1	1
Peru	Silvia Neciosup	00205	1	1
USA	Mark Gregory Goldstein	00234	1	0
Mexico	Luis Alfonso Adel	00249	1	0
Israel	Wilmosh Mermershtain	00252	1	1
Israel	Avishay Sella	00262	1	1
Czech Republic	Vera Hejzlarova	00267	1	1