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Article

Circulating Tumor DNA Early Kinetics Predict Response of Metastatic Melanoma to Anti-PD1 Immunotherapy: Validation Study

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Table S1. Characteristics of first-line patients.

	Total	**Undetectable Baseline ctDNA**	**Detectable Baseline ctDNA**	***p***
n ($n_{derivation}$ + $n_{validation}$)	58 (26 + 32)	33 (14 + 19)	25 (12 + 13)	-
Age m (Q1—Q3)	65.5 (59.5—75.7)	66.6 (60.4—79)	64.1 (59—72)	0.520
Tumor thickness m (Q1—Q3)	3.6 (1.6—5)	3.3 (1.7—4.9)	4 (1.4—5.8)	0.862
Number of metastases m (Q1—Q3)	2.8 (2.0—3.8)	2.1 (2—2)	3.8 (2—5)	<0.0001
Baseline LDH IU/L; m (Q1—Q3)	381.0 (180.1—414.5)	204.3 (174—227.2)	539.9 (203—516.5)	0.003

		Total	**Undetectable Baseline ctDNA**	**Detectable Baseline ctDNA**	***p***
Gender	M	22	7 (32%)	15 (68%)	0.006
	F	36	26 (72%)	10 (28%)	
Stage	III	24	19 (79%)	5 (21%)	0.007
	IV	34	14 (41%)	20 (59%)	
Ulceration	Yes	21	11 (52%)	10 (48%)	0.848
	No	21	13 (62%)	8 (38%)	
Presence of lymph node metastasis	Yes	41	19 (46%)	22 (54%)	0.019
	No	17	14 (82%)	3 (18%)	
Presence of cutaneous metastasis	Yes	33	19 (58%)	14 (42%)	1.000
	No	25	14 (56%)	11 (44%)	
Presence of pulmonary metastasis	Yes	14	5 (36%)	9 (64%)	0.120
	No	44	28 (64%)	16 (36%)	
Presence of cerebral metastasis	Yes	6	3 (50%)	3 (50%)	1.000
	No	52	30 (58%)	22 (42%)	
Presence of abdominal metastasis	Yes	15	3 (20%)	12 (80%)	0.002
	No	43	30 (70%)	13 (30%)	
Presence of bone metastasis	Yes	15	2 (13%)	13 (87%)	0.0002
	No	43	31 (72%)	12 (28%)	
Mutated gene	NRAS	51	28 (55%)	23 (45%)	0.687
	BRAF	7	5 (71%)	2 (29%)	
Baseline LDH	≥426 IU/L (2x ULN)	9	0	9 (100%)	0.001
	<426 IU/L (2x ULN)	29	18 (62%)	11 (38%)	
	Undetermined	20	15 (75%)	5 (25%)	
Treatment	Nivolumab monotherapy	51	30 (59%)	21 (41%)	0.450
	Nivolumab + Ipilimumab	7	3 (43%)	4 (57%)	

ULN: upper limit of normal

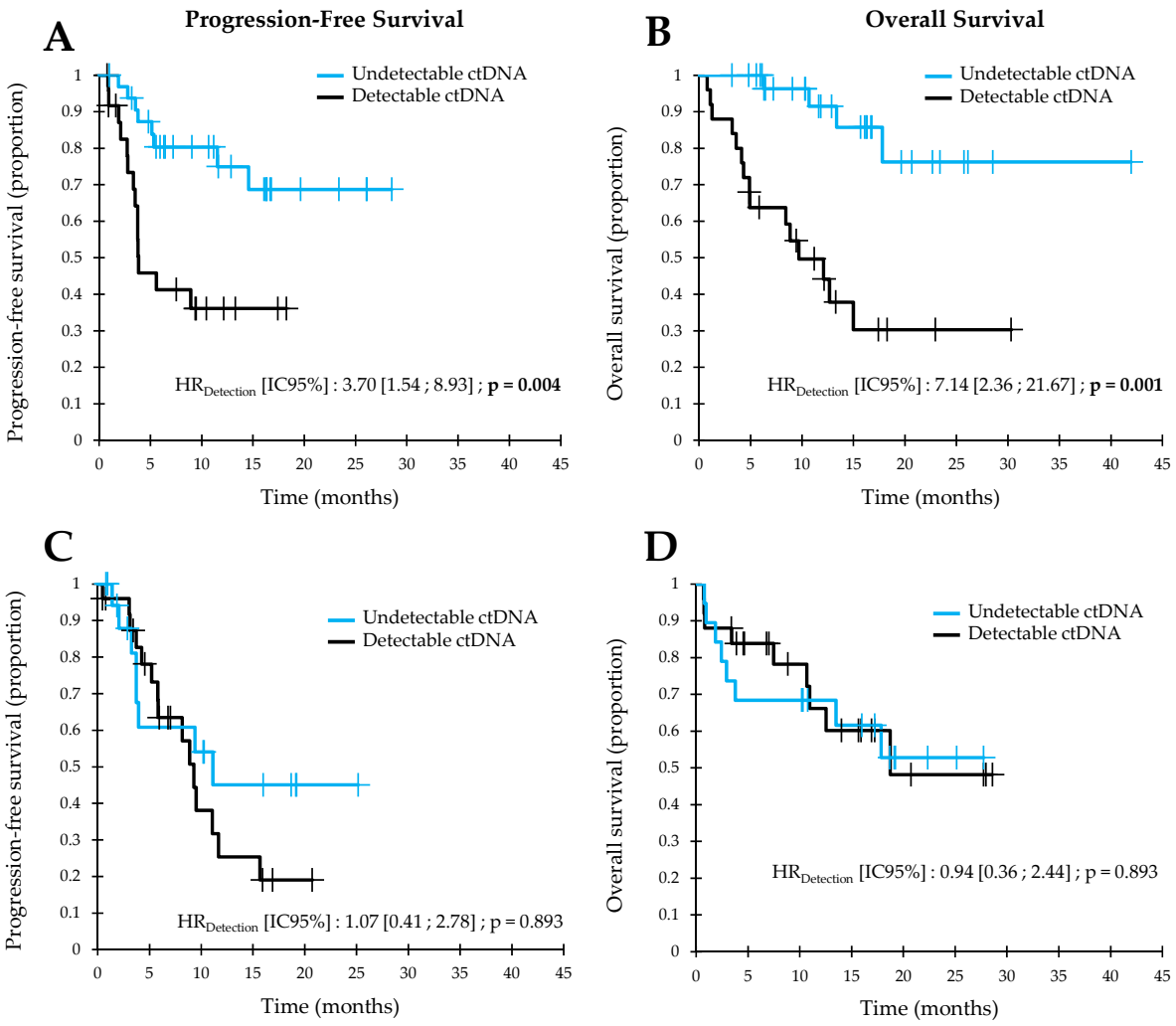

Figure S1. Prognostic value of baseline ctDNA detection in pooled analysis : Kaplan-Meier estimate of the PFS **(A)** and OS **(B)** depending on ctDNA detection at the initiation of first-line immunotherapy; Kaplan-Meier estimate of PFS **(C)** and OS **(D)** depending on ctDNA detection at the initiation of an immunotherapy beyond the first line.

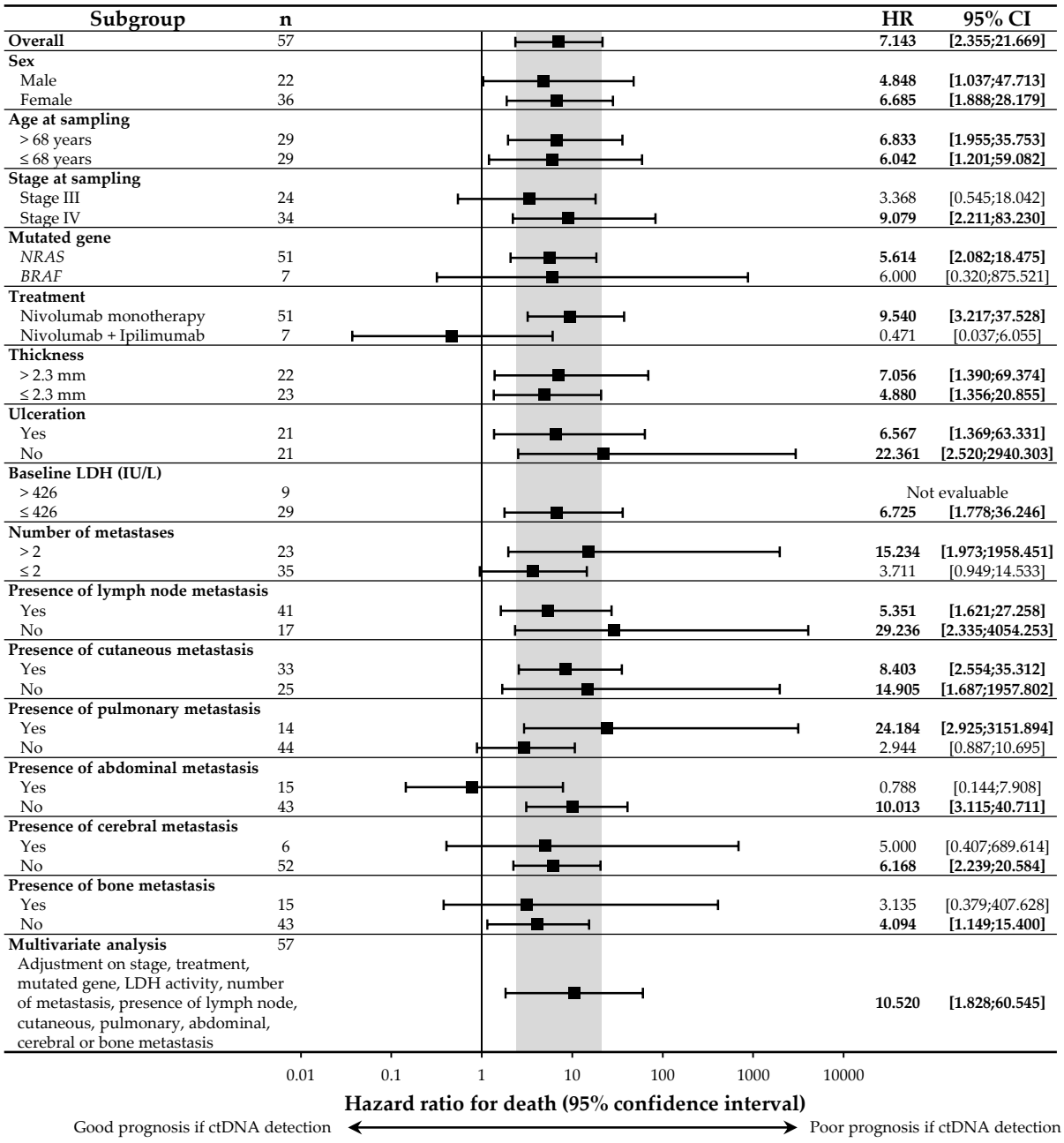

Figure S2. Forest plot of OS in subgroup and multivariate analysis, according to ctDNA detectability at the initiation of first-line immunotherapy.

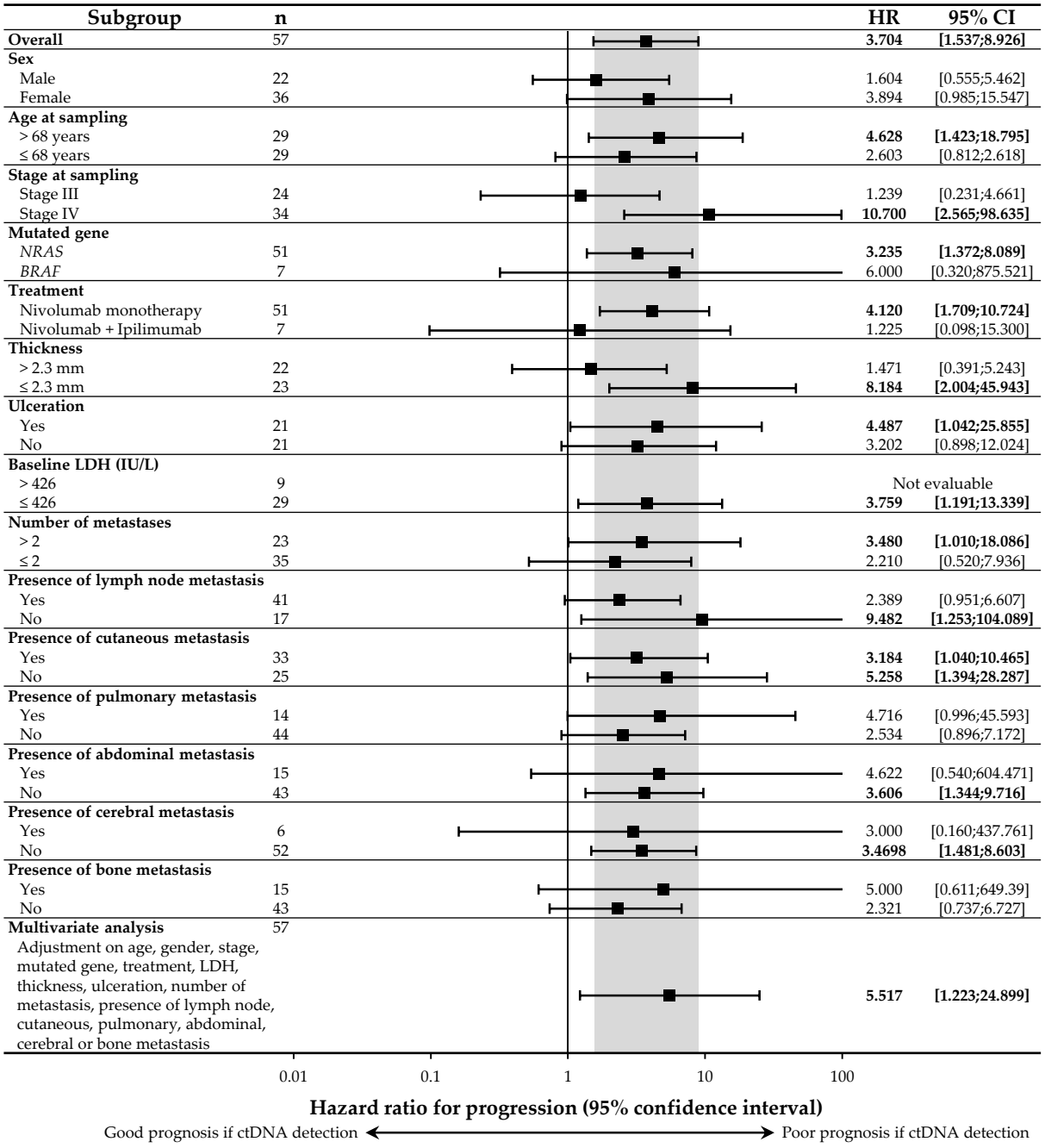

Figure S3. Forest plot of PFS in subgroup and multivariate analysis, according to ctDNA detectability at the initiation of first-line immunotherapy.