

Supplementary materials

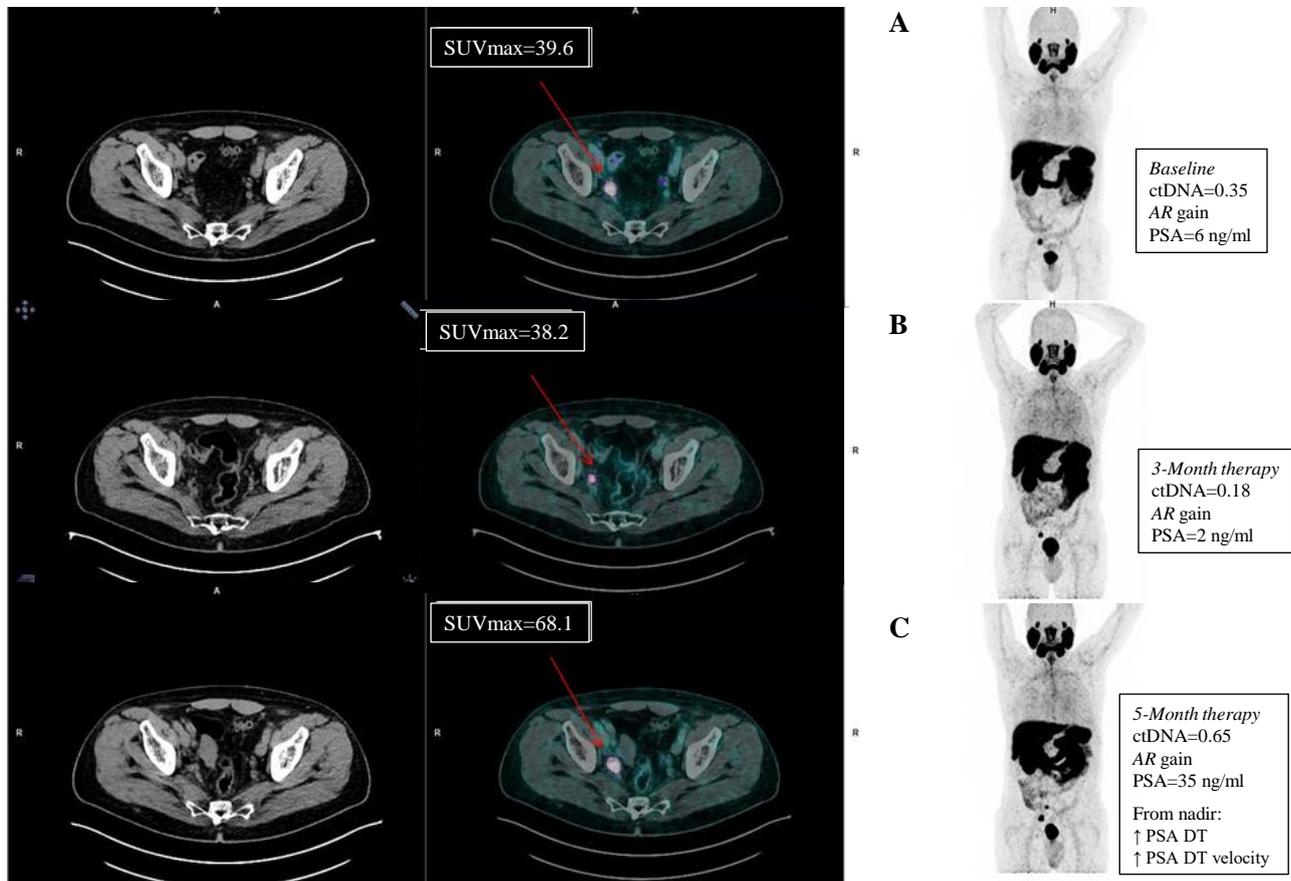


Figure S1. A representative case of the association between baseline high ctDNA and AR gain with increased PSA DT and PSA velocity at 5-month abiraterone treatment. Baseline ctDNA high and AR gain correlate with a shorter time to PSA, a faster PSA DT from nadir, as well as a significant higher PSA DT velocity from nadir. This patient belongs to the cohort characterized by a worst prognosis. *Abbreviations:* AR, androgen receptor; PSA DT, prostate specific antigen doubling time; ctDNA, plasma tumor DNA.

Table S1. Univariate analysis of PFS and OS

	PFS		OS	
	HR (95% CI)	p	HR (95% CI)	p
logPSA (continuous variable)	1.23 (1.14-1.32)	<0.0001	1.25 (1.16-1.35)	<0.0001
Age (≥ 74 vs <74)	1.03 (0.79-1.35)	0.803	0.98 (0.74-1.29)	0.881
Bone metastasis (yes vs no)	1.35 (0.91-2.01)	0.135	1.60 (1.05-2.45)	0.030
Lymph nodes metastasis (yes vs no)	1.01 (0.76-1.32)	0.978	0.92 (0.70-1.22)	0.586
Visceral metastasis (yes vs no)	1.87 (1.30-2.68)	0.0007	2.47 (1.71-3.58)	<0.0001
Liver metastasis (yes vs no)	2.59 (1.56-4.30)	0.0002	3.17 (1.89-5.32)	<0.0001
Lung metastasis (yes vs no)	1.24 (0.73-2.11)	0.416	1.73 (1.02-2.93)	0.043
Other metastasis (yes vs no)	1.66 (0.90-3.07)	0.104	1.96 (1.06-3.62)	0.032
Previous therapy (enza vs abi)	1.47 (1.11-1.94)	0.007	1.20 (0.90-1.59)	0.220
Previous chemotherapy (yes vs no)	1.98 (1.46-2.68)	<0.0001	2.11 (1.53-2.90)	<0.0001
Prostatectomy (yes vs no)	0.71 (0.54-0.94)	0.015	0.76 (0.57-1.01)	0.055
Radioterapy (yes vs no)	1.01 (0.74-1.38)	0.940	1.03 (0.74-1.42)	0.859
ECOG PS (2 vs 0-1)	3.26 (1.91-5.57)	<0.0001	5.88 (3.39-10.22)	<0.0001
Gleason score (≥ 8 vs 6-7)	1.10 (0.83-1.47)	0.513	1.05 (0.78-1.41)	0.765
AR CN (Gain vs Normal)	2.66 (1.98-3.58)	<0.0001	3.02 (2.22-4.11)	<0.0001
ctDNA (>0.180 vs ≤ 0.180)	2.41 (1.71-3.38)	<0.0001	2.20 (1.55-3.12)	<0.0001
ALP (≥ 129 vs <129)	1.83 (1.39-2.42)	<0.0001	2.12 (1.59-2.83)	<0.0001
Albumin (<4 vs ≥ 4)	0.70 (0.53-0.92)	0.012	0.61 (0.46-0.81)	0.0007
Hemoglobin (<12.5 vs ≥ 12.5)	1.45 (1.08-1.94)	0.014	1.69 (1.24-2.30)	0.0009
CgA (≥ 120 vs <120)	1.49 (1.25-1.78)	<0.0001	1.83 (1.52-2.21)	<0.0001
LDH (≥ 225 vs <225)	2.61 (1.92-3.56)	<0.0001	2.68 (1.97-3.66)	<0.0001
NLR (≥ 3 vs <3)	1.50 (1.15-1.96)	0.003	1.47 (1.11-1.94)	0.006
PSA DT from nadir (continuous variable)	0.92 (0.89-0.96)	<0.0001	0.94 (0.91-0.98)	0.002
PSA DT velocity from nadir (continuous variable)	1.001 (1.001-1.002)	<0.0001	1.001 (1.001-1.002)	<0.0001

Abbreviations: ALP, alkaline phosphatase; AR CN, androgen receptor copy number; CgA, chromogranin A; ; ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; NLR, neutrophil-lymphocyte ratio; PS, performance status; PSA DT, prostate specific antigen doubling time; ctDNA, circulating tumor DNA.