



Fig S1. Progression-free survival on treatment with abiraterone acetate and *HSD3B1* genotype.

Table S2. Metabolite concentrations (ng/ml) according to *HSD3B1* genotype in patients with castration-resistant prostate cancer

Genotype	Dose to Draw (H:Min)*	Treatment Duration (Months)	Abiraterone	D4A	3-Keto-5 α -Abi	3 α -OH-5 α -Abi	3 β -OH-5 α -Abi	3-Keto-5 β -Abi	3 α -OH-5 β -Abi	3 β -OH-5 β -Abi
WT 1	01:30	24	15.75	0.96	6.99	1.77	0.58	7.08	10.19	22.54
WT 2	02:15	2	65.09	3.66	1.73	0.30	0.27	8.72	8.01	19.39
WT 3	02:15	12	39.98	1.28	3.46	0.23	0.11	6.46	2.04	3.08
WT 4	02:20	1	105.62	3.69	6.64	0.89	0.68	16.27	24.48	19.87
WT 5	05:00	8	12.96	0.77	2.25	0.48	0.16	2.50	3.98	6.75
WT 6	07:30	13	21.50	1.29	1.04	0.26	0.12	4.48	5.52	12.54
WT 7	10:45	5	19.24	0.52	1.22	0.37	0.15	1.28	3.83	4.33
WT 8	14:45	11	52.70	3.15	3.11	1.15	0.44	2.37	9.17	7.58
HZ 1	02:00	32	8.64	1.28	1.36	0.42	0.12	2.43	6.46	9.42
HZ 2	02:15	39	40.49	2.05	9.07	1.30	0.39	4.37	4.90	5.71
HZ 3	02:30	26	48.45	1.29	10.66	1.16	0.52	5.95	3.44	6.86
HZ 4	03:15	21	70.67	3.85	8.80	1.98	0.53	5.85	9.06	10.89
HZ 5	05:00	3	81.90	4.11	6.73	1.13	0.40	21.74	22.28	19.10
HZ 6	05:15	3	56.45	3.17	7.66	1.74	0.54	7.63	14.58	19.10
HZ 7	05:30	1	53.39	1.06	7.71	0.88	0.33	5.47	2.71	4.22
HZ 8	06:15	3	14.97	1.58	3.70	0.92	0.28	6.94	8.72	10.84
HZ 9	06:45	1	43.41	3.67	20.48	5.87	4.14	12.74	22.04	19.06
HZ 10	08:30	2	16.71	1.25	8.10	1.93	0.45	8.08	9.84	15.19
HZ 11	09:30	1	33.65	1.54	3.21	1.22	0.35	0.83	2.45	2.06
HZ 12	09:30	1	23.67	2.42	2.49	0.65	0.19	4.22	6.71	5.94
HZ 13	10:30	39	60.64	2.49	10.96	2.82	0.78	7.15	11.11	10.76
HZ 14	11:30	2	38.90	2.58	4.65	1.29	0.53	6.69	10.37	11.87
HZ 15	11:45	22	6.02	0.75	0.13	0.10	0.10	1.52	3.30	3.33
HZ 16	12:00	5	67.98	3.59	5.36	1.11	0.44	16.54	12.53	27.29
HZ 17	12:15	11	41.22	3.71	11.04	2.27	0.77	25.76	21.59	37.91
HZ 18	12:15	25	19.06	1.14	4.66	1.21	0.34	11.54	10.95	12.50
HZ 19	15:45	2	66.69	2.83	8.71	2.88	0.88	4.29	10.53	12.34
MT 1	08:15	21	61.47	4.54	9.88	1.73	0.60	14.77	11.85	24.32
MT 2	12:15	8	52.41	3.17	10.89	2.83	0.88	8.97	10.57	19.10
MT 3	14:15	5	31.48	3.07	20.28	6.42	1.99	7.89	19.94	15.87

*Time from last AA dose to blood draw

WT = wild-type

HZ = heterozygous mutant

MT = homozygous mutant

Table S3. Polyserial correlation of normalized abiraterone metabolite concentrations (ng/mL) and *HSD3B1* genotype based on normalization to the 4 hour PK time point.

Abiraterone/metabolite	WT (8 pts)	HZ (19 pts)	MT (3 pts)	Correlation coefficient (ρ)	p-value
Abiraterone	35.53	56.51	26.15	0.04	0.85
D4A	0.29	0.50	0.17	0.15	0.48
3-keto-5 α -Abi	0.07	7.05	7.35	0.49	0.002
3 α -OH-5 α -Abi	0.05	1.11	1.64	0.56	0.0001
3 β -OH-5 α -Abi	0.12	0.39	0.80	0.46	0.006
3-keto-5 β -Abi	0.15	0.64	0.17	0.13	0.55
3 α -OH-5 β -Abi	0.49	0.80	1.66	0.31	0.10
3 β -OH-5 β -Abi	0.46	1.29	0.91	0.17	0.41

Table S4. Results from Anova test and Tukey's Honest Significant Difference (HSD) pairwise comparisons of mean metabolite concentration values between genotypes (including point estimates of mean differences and their 95% confidence intervals)

Abiraterone/ metabolite	ANOVA p-value	Tukey's Honest Significant Difference (HSD)		
		HZ – WT [95% CI]	MT – WT [95% CI]	MT – HZ [95% CI]
Abiraterone	0.674	6.45 [-14.2, 27.1]	-2.19 [-35.4, 31.0]	-8.64 [-39.1, 21.9]
D4A	0.661	0.09 [-0.14, 0.33]	0.07 [-0.32, 0.45]	-0.03 [-0.38, 0.32]
3-keto-5 α -Abi	0.044	2.14 [0.17, 4.10]	2.51 [-0.65, 5.67]	0.37 [-2.53, 3.27]
3 α -OH-5 α -Abi	0.025	0.89 [0.07, 1.70]	1.35 [0.05, 2.66]	0.47 [-0.73, 1.67]
3 β -OH-5 α -Abi	0.107	0.23 [-0.07, 0.53]	0.40 [-0.08, 0.87]	0.16 [-0.28, 0.60]
3-keto-5 β -Abi	0.785	0.11 [-0.26, 0.49]	0.10 [-0.51, 0.70]	-0.01 [-0.57, 0.54]
3 α -OH-5 β -Abi	0.347	0.33 [-0.29, 0.94]	0.54 [-0.44, 1.52]	0.21 [-0.69, 1.12]
3 β -OH-5 β -Abi	0.748	0.51 [-1.74, 2.74]	1.13 [-2.47, 4.74]	0.63 [-2.68, 3.93]

Table S5. P-values before multiple testing correction and their false discovery rates (FDRs) calculated by Benjamini and Hochberg method*

Abiraterone/metabolite	p-values from individual tests	FDR
Abiraterone	0.850	0.850
D4A	0.476	0.623
3-keto-5 α -Abi	0.0025	0.01
3 α -OH-5 α -Abi	0.00012	0.00094
3 β -OH-5 α -Abi	0.00667	0.0178
3-keto-5 β -Abi	0.546	0.623
3 α -OH-5 β -Abi	0.0958	0.192
3 β -OH-5 β -Abi	0.411	0.623

*Benjamini, Yoav; Hochberg, Yosef (1995). "Controlling the false discovery rate: a practical and powerful approach to multiple testing". Journal of the Royal Statistical Society, Series B. 57 (1): 289–300.