**Supplementary Table S1.** Univariable and multivariable Cox proportional hazards models assessing association of PGA and specific genetic alterations with biochemical recurrence

|  |  |  |
| --- | --- | --- |
| **Variable** | **Univariable** | **Multivariable\*** |
|  | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| PGA (continuous) ‡ | 1.03 (0.99, 1.06) | 0.075 | 1.01 (0.97, 1.04) | 0.684 |
| PGA (quartile)^ ≤25th percentile 25-50th percentile 50-75th percentile >75th percentile | 1.00 (reference)1.09 (0.58, 2.05)0.89 (0.45, 1.79)1.91 (1.06, 3.45) | --0.7930.754**0.032** | 1.00 (reference)0.90 (0.47, 1.73)0.71 (0.34, 1.47)1.11 (0.58, 2.09) | --0.7460.3520.758 |
| *CDKN1B* deep deletion | 1.96 (0.79, 4.92) | 0.149 | 1.26 (0.49, 3.22) | 0.633 |
| *CHD1*deep deletion | 0.66 (0.16, 2.69) | 0.562 | 0.88 (0.21, 3.70) | 0.865 |
| *PTEN* deep deletion | 4.45 (1.76, 11.25) | **0.002** | 2.94 (1.08, 8.00) | **0.035** |
| *FOXA1* mutation | 0.85 (0.37, 1.97) | 0.710 | 0.61 (0.26, 1.44) | 0.259 |
| *SPOP* mutation | 0.61 (0.28, 1.33) | 0.210 | 0.75 (0.33, 1.71) | 0.497 |
| *TP53* mutation | 2.36 (0.95, 5.89) | 0.065 | 1.49 (0.58, 3.82) | 0.407 |

\*Multivariable models were adjusted for age at RP, PSA, RP grade group <4 or ≥4, and pathologic stage. RP grade group was analyzed as dichotomous variable due to low number of metastatic events per grade group.

‡ Per 1% change in PGA

^≤0.93% (≤25th percentile), 0.94-3.74% (25th-50th percentile), 3.75-9.35% (50th-75th percentile), and >9.35% (>75th percentile)

**Supplementary Table S2.** Clinico-pathologic characteristics for JHMI AA cohort (n=205) and TCGA cohort (n=313).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **JHMI AA (n=205)** | **TCGA AA (n=43)** | **TCGA EA (n=270)** | **P-value: JHMI AA vs. TCGA EA** | **P-value: TCGA AA vs. TCGA EA** |
| Median age, yr (IQR) | 58 (53-63) | 56 (53-64) | 62 (57-66) | **<0.001** | **0.004** |
| Median PSA, ng/ml (IQR) | 7.30 (5.24-13.00) | 8.55 (5.50-14.90) | 7.20 (5.00-11.60) | 0.637 | 0.340 |
| RP grade group, n (%) 1 (GS 6) 2 (GS 3+4) 3 (GS 4+3) 4 (GS 8) 5 (GS 9-10) | 28 (13.7)32 (15.6)91 (44.4)33 (16.1)21 (10.2) | 12 (27.9)14 (32.6)8 (18.6)5 (11.6)4 (9.3) | 47 (17.4)82 (30.4)67 (24.8)36 (13.3)38 (14.1) | **<0.001** | 0.472 |

**Supplementary Table S3.** Clinico-pathologic characteristics for JHMI AA cohort with all available genetic and clinical outcome data (n=184).

|  |  |
| --- | --- |
| **Variable** | **AA (n=184)** |
| Median PSA, ng/ml (IQR) | 7.30 (5.30-13.05) |
| Median age, yr (IQR) | 58 (53-63) |
| Clinical T stage, n (%) T1c T2a T2b/c | 138 (75.0)31 (16.9)15 (8.2) |
| Biopsy grade group, n (%) 1 (GS 6) 2 (GS 3+4) 3 (GS 4+3) 4 (GS 8) 5 (GS 9-10) | 65 (35.3)43 (23.4)42 (22.8)24 (13.0)10 (5.4) |
| RP grade group, n (%) 1 (GS 6) 2 (GS 3+4) 3 (GS 4+3) 4 (GS 8) 5 (GS 9-10) | 25 (13.6)30 (16.3)82 (44.6)30 (16.3)17 (9.2) |
| Pathologic T stage, n (%) T2N0 T3aN0 T3bN0 N1 | 79 (43.7)63 (34.8)24 (13.3)15 (18.3) |
| Median length of follow-up, yr (IQR) | 6 (2-10) |
| Biochemical recurrence, n (%) | 71 (41.3) |
| 5-yr BCR-free survival (95% CI)10-yr BCR-free survival (95% CI) | 0.586 (0.497, 0.665)0.439 (0.334, 0.539) |
| Metastasis, n (%) | 20 (11.6) |
| 5-yr metastasis-free survival (95% CI)10-yr metastasis-free survival (95% CI) | 0.912 (0.841, 0.952)0.800 (0.687, 0.876) |

**Supplementary Table S4.** Distribution of most common mutations and copy number alterations (deep deletions or high level amplifications) in JHMI AA cohort (n=205).

|  |  |  |  |
| --- | --- | --- | --- |
| **Genetic alteration** | **Mutation, n (%)** | **CNA, high level amplification and/or deep deletion, n (%)** | **Total, n (%)** |
| Any alteration identified | 84 (41.0) | 59 (28.8) | 143 (69.8)  |
| SPOP | 23 (11.2) | 0 (0) | 23 (11.2) |
| FOXA1 | 17 (8.3) | 4 (2.0) | 21 (10.2) |
| CDKN1B | 0 (0) | 13 (6.3) | 13 (6.3) |
| CHD1 | 3 (1.5) | 9 (4.4) | 12 (5.9) |
| PTEN | 1 (0.5) | 7 (3.4) | 8 (3.9) |
| TP53 | 8 (3.9) | 0 (0) | 8 (3.9) |
| NKX3-1 | 1 (0.5) | 7 (3.4) | 8 (3.9) |
| BRAF | 4 (2.0) | 1 (0.5) | 5 (2.4) |
| BRCA2 | 5 (2.4) | 0 (0) | 5 (2.4) |
| MYC | 0 (0) | 5 (2.4) | 5 (2.4) |
| PTPN14 | 1 (0.5) | 4 (2.0) | 5 (2.4) |
| CDK12 | 3 (1.5) | 1 (0.5) | 4 (2.0) |
| IDH1 | 4 (2.0) | 0 (0) | 4 (2.0) |
| TCEB1 | 0 (0)s | 4 (2.0) | 4 (2.0) |
| YWHAZ | 0 (0) | 4 (2.0) | 4 (2.0) |
| ZMYM3 | 4 (2.0) | 0 (0) | 4 (2.0) |
| APC | 2 (1.0) |  0 (0) |  2 (1.0) |
| HRAS | 2 (1.0) | 0 (0) | 2 (1.0) |
| PIK3CA | 2 (1.0) | 0 (0) | 2 (1.0) |
| ERF  | 0 (0) | 1 (0.5) | 1 (0.5) |
| MED12 | 1 (0.5) | 0 (0) | 1 (0.5) |
| MSH2  | 1 (0.5) | 0 (0) | 1 (0.5) |
| SETD2 | 1 (0.5) | 0 (0) | 1 (0.5) |
| TSC2  | 1 (0.5) | 0 (0) | 1 (0.5) |

**Supplementary Table S5.** List of mutations detected with associated variant allele frequencies.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **SAMPLE** | **Gene** | **Mutation** | **Classification** | **Variant fraction** |
| Lotan1 | **SPOP** | p.Y87N | nonsynonymousSNV | **0.3901** |
| Lotan101 | **SPOP** | p.F133L | nonsynonymousSNV | **0.4094** |
| Lotan107 | **IDH1** | p.R132G | nonsynonymousSNV | **0.1272** |
| Lotan111 | **SPOP** | p.F102V | nonsynonymousSNV | **0.2111** |
| Lotan118 | **SPOP** | p.F133V | nonsynonymousSNV | **0.1468** |
| Lotan12 | **BRAF** | p.K601E | nonsynonymousSNV | **0.3171** |
| Lotan120 | **TP53** | p.C106S | nonsynonymousSNV | **0.0925** |
| Lotan122 | **TP53** | p.123\_124del | nonframeshiftdeletion | **0.3224** |
| Lotan129 | **SPOP** | p.F133V | nonsynonymousSNV | **0.2265** |
| Lotan13 | **SPOP** | p.F125C | nonsynonymousSNV | **0.1073** |
| Lotan131 | **FOXA1** | p.263\_268del | nonframeshiftdeletion | **0.3288** |
| Lotan131 | **IDH1** | p.R132L | nonsynonymousSNV | **0.3023** |
| Lotan132 | **MSH2** | p.Q681X | stopgainSNV | **0.1935** |
| Lotan135 | **FOXA1** | p.F266L | nonsynonymousSNV | **0.2488** |
| Lotan144 | **SPOP** | p.F133L | nonsynonymousSNV | **0.1505** |
| Lotan153 | **PTEN** | p.E73fs | frameshiftdeletion | **0.1994** |
| Lotan157 | **TP53** | p.R64P | nonsynonymousSNV | **0.3597** |
| Lotan158 | **SPOP** | p.F133L | nonsynonymousSNV | **0.1919** |
| Lotan161 | **BRCA2** | p.V2620fs | frameshiftdeletion | **0.2883** |
| Lotan164 | **SPOP** | p.F102V | nonsynonymousSNV | **0.156** |
| Lotan17 | **FOXA1** | p.H247Y | nonsynonymousSNV | **0.3412** |
| Lotan17 | **IDH1** | p.R132C | nonsynonymousSNV | **0.3331** |
| Lotan171 | **CDK12** | p.Q612X | stopgainSNV | **0.351** |
| Lotan171 | **ZMYM3** | p.L82fs | frameshiftinsertion | **0.751** |
| Lotan176 | **BRCA2** | p.S662fs | frameshiftdeletion | **0.3431** |
| Lotan177 | **SPOP** | p.F102C | nonsynonymousSNV | **0.1978** |
| Lotan179 | **FOXA1** | p.F266L | nonsynonymousSNV | **0.3208** |
| Lotan179 | **SPOP** | p.F102C | nonsynonymousSNV | **0.0961** |
| Lotan18 | **MED12** | p.L1224F | nonsynonymousSNV | **0.4661** |
| Lotan180 | **SPOP** | p.W131G | nonsynonymousSNV | **0.3305** |
| Lotan20 | **SPOP** | p.F133L | nonsynonymousSNV | **0.21** |
| Lotan20 | **ZMYM3** | p.K665fs | frameshiftdeletion | **0.3657** |
| Lotan22 | **BRAF** | p.K601E | nonsynonymousSNV | **0.3461** |
| Lotan22 | **FOXA1** | p.D226H | nonsynonymousSNV | **0.4561** |
| Lotan23 | **BRAF** | p.K601N | nonsynonymousSNV | **0.3882** |
| Lotan23 | **FOXA1** | p.F266V | nonsynonymousSNV | **0.2397** |
| Lotan25 | **FOXA1** | p.267\_274del | nonframeshiftdeletion | **0.1919** |
| Lotan27 | **ZMYM3** | p.R1117X | stopgainSNV | **0.3344** |
| Lotan28 | **PIK3CA** | p.E542V | nonsynonymousSNV | **0.1194** |
| Lotan3 | **ATM** | p.Q893X | stopgainSNV | **0.7284** |
| Lotan3 | **HRAS** | p.Q61L | nonsynonymousSNV | **0.8445** |
| Lotan3 | **TP53** | p.P146A | nonsynonymousSNV | **0.2322** |
| Lotan31 | **SPOP** | p.F133L | nonsynonymousSNV | **0.1136** |
| Lotan32 | **SPOP** | p.F133V | nonsynonymousSNV | **0.3518** |
| Lotan35 | **CDK12** | p.893\_894del | frameshiftdeletion | **0.2092** |
| Lotan39 | **FOXA1** | p.H247R | nonsynonymousSNV | **0.363** |
| Lotan4 | **TP53** | p.P21fs | frameshiftdeletion | **0.257** |
| Lotan4 | **TP53** | p.R210X | stopgainSNV | **0.3177** |
| Lotan46 | **ZMYM3** | p.425\_428del | frameshiftdeletion | **0.6563** |
| Lotan47 | **FOXA1** | p.R261H | nonsynonymousSNV | **0.2704** |
| Lotan49 | **CDK12** | p.R858Q | nonsynonymousSNV | **0.2449** |
| Lotan49 | **CDK12** | p.Q165X | stopgainSNV | **0.3465** |
| Lotan5 | **PTPN14** | p.L28fs | frameshiftdeletion | **0.3864** |
| Lotan53 | **CHD1** | p.N1524fs | frameshiftdeletion | **0.3675** |
| Lotan53 | **SPOP** | p.W131G | nonsynonymousSNV | **0.2862** |
| Lotan54 | **TP53** | p.P20L | nonsynonymousSNV | **0.7262** |
| Lotan55 | **PIK3CA** | p.H1047R | nonsynonymousSNV | **0.224** |
| Lotan56 | **BRCA2** | p.2262\_2269del | frameshiftdeletion | **0.0898** |
| Lotan57 | **SPOP** | p.F133C | nonsynonymousSNV | **0.1661** |
| Lotan6 | **BRCA2** | p.K944X | stopgainSNV | **0.6865** |
| Lotan63 | **CHD1(NM\_001270:****exon5:c.437+2T>G)** | NA | splice siteSNV | **0.3134** |
| Lotan64 | **BRAF** | p.K601E | nonsynonymousSNV | **0.3525** |
| Lotan64 | **FOXA1** | p.E255K | nonsynonymousSNV | **0.624** |
| Lotan64 | **FOXA1** | p.D226N | nonsynonymousSNV | **0.6118** |
| Lotan65 | **FOXA1** | p.F254C | nonsynonymousSNV | **0.239** |
| Lotan67 | **FOXA1** | p.262\_267del | nonframeshiftdeletion | **0.0563** |
| Lotan68 | **SPOP** | p.F102C | nonsynonymousSNV | **0.3063** |
| Lotan74 | **SPOP** | p.F133V | nonsynonymousSNV | **0.3204** |
| Lotan79 | **APC** | p.S578fs;p.S596fs;p.S596fs | frameshiftdeletion | **0.3672** |
| Lotan79 | **FOXA1** | p.E255fs | frameshiftdeletion | **0.2249** |
| Lotan82 | **APC** | p.388\_389del | frameshiftdeletion | **0.3196** |
| Lotan82 | **FOXA1** | p.R262S | nonsynonymousSNV | **0.3455** |
| Lotan82 | **SETD2** | p.S1682X | stopgainSNV | **0.2929** |
| Lotan82 | **SPOP** | p.F102C | nonsynonymousSNV | **0.3458** |
| Lotan82 | **TSC2** | p.F846fs | frameshiftdeletion | **0.2963** |
| Lotan83 | **SPOP** | p.F102V | nonsynonymousSNV | **0.3301** |
| Lotan85 | **FOXA1** | p.324\_330del | frameshiftdeletion | **0.1495** |
| Lotan90 | **FOXA1** | p.320\_321del | frameshiftdeletion | **0.1075** |
| Lotan90 | **SPOP** | p.K129E | nonsynonymousSNV | **0.0582** |
| Lotan91 | **SPOP** | p.F102V | nonsynonymousSNV | **0.2258** |
| Lotan94 | **HRAS** | p.Q61R | nonsynonymousSNV | **0.2526** |
| Lotan98 | **TP53** | p.S109T | nonsynonymousSNV | **0.1935** |
| Lotan99 | **TP53** | p.Q4X | stopgainSNV | **0.6895** |
| Sample217 | **FOXA1** | p.G257D | nonsynonymousSNV | **0.1415** |
| Sample219 | **NKX3-1** | p.56\_58del | nonframeshiftdeletion | **0.2353** |