**Supplementary Table S1.** Biomarkers evaluated

|  |  |  |
| --- | --- | --- |
| **Biomarker**  | **Sample type** | **Time point** |
| AR/ER/PR/HER2 expressiona, b  | FFPET  | Baseline |
| CYP17/CYP19 expressiona | FFPET  | Baseline |
| Ki-67 expressiona | FFPET  | Baseline |
| AR/ER expressionc | CTC | Baseline, C2D1, EOT |
| AR amplificationd | CTC | Baseline, EOT |
| HER2 amplificationd | CTC | Baseline, EOT |
| Ki-67 expressionc | CTC | Baseline, C2D1 |

aAssessed by IHC.
bPR expression was only assessed for patients with ER+/HER2– status.

cAssessed by immunofluorescence.

dAssessed by FISH.

Cutpoints for positive expression: AR, 10%; ER, 1%; PR, 1%; HER2, 1%; CYP17, 1%; CYP19, 1%; Ki-67, 10%.

AR, androgen receptor; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; FFPET, formalin-fixed paraffin-embedded tissue; CTC, circulating tumor cell; C2D1, cycle 2 day 1; EOT, end of treatment; IHC, immunohistochemistry.

**Supplementary Table S2.** Additional biomarker associations with PFS by treatment

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker** | **Class level** | **Treatment** | **Event/Total (%)** | **Median (95% CI)** | ***P* value** | **HR(95% CI)** |
| CTC ER  | Positive (≥ 1%) | E | 14/15 (93.3) | 1.9 (1.7 to 3.6) | – | – |
| AA | 14/18 (77.8) | 3.5 (1.9 to 4.5) | 0.38 | 0.71 (0.34 to 1.51) |
| AAE | 16/19 (84.2) | 3.6 (1.9 to 5.6) | 0.24 | 0.64 (0.31 to 1.34) |
| AA and AAE | 30/37 (81.1) | 3.5 (1.9 to 4.5) | 0.23 | 0.68 (0.36 to 1.28) |
| CTC AR and ER combination | CTC AR+ (≥ 10%) and ER+ (≥ 1%) | E | 10/11 (90.9) | 1.9 (1.6 to 5.3) | – | – |
| AA | 10/14 (71.4) | 3.5 (1.9 to 5.5) | 0.45 | 0.71 (0.29 to 1.72) |
| AAE | 10/13 (76.9) | 3.7 (3.6 to 6.8) | 0.07 | 0.41 (0.16 to 1.07) |
| AA and AAE | 20/27 (74.1) | 3.7 (3.5 to 5.6) | 0.19 | 0.59 (0.27 to 1.29) |
| FFPET Ki-67  | Positive (≥ 10%) | E | 49/67 (73.1) | 3.7 (1.9 to 5.6) | – | – |
| AA | 49/58 (84.5) | 3.6 (1.9 to 4.9) | 0.07 | 1.45 (0.97 to 2.18) |
| AAE | 54/70 (77.1) | 4.2 (3.6 to 5.6) | 0.88 | 1.03 (0.70 to 1.52) |
| AA and AAE | 103/128 (80.5) | 3.9 (3.6 to 5.5) | 0.27 | 1.22 (0.86 to 1.72) |
| Estrone | Low (< Median) | E | 38/45 (84.4) | 1.9 (1.8 to 3.5) | – | – |
| AA | 32/41 (78.0) | 3.6 (1.9 to 5.7) | 0.35 | 0.79 (0.49 to 1.29) |
| AAE | 45/52 (86.5) | 4.2 (3.6 to 6.6) | 0.07 | 0.67 (0.43 to 1.04) |
| AA and AAE | 77/93 (82.8) | 3.7 (3.5 to 5.6) | 0.09 | 0.71 (0.48 to 1.05) |
| CTC Ki-67  | Positive (≥ 10%) | E | 12/12 (100.0) | 1.9 (1.7 to 1.9) | – | – |
|  |  | AA | 17/21 (81.0) | 1.9 (1.6 to 3.9) | 0.11 | 0.50 (0.22 to 1.15) |
|  |  | AAE | 16/19 (84.2) | 3.7 (1.9 to 5.6) | 0.003 | 0.26 (0.11 to 0.64) |
|  |  | AA and AAE | 33/40 (82.5) | 3.5 (1.9 to 3.9) | 0.007 | 0.36 (0.17 to 0.76) |
| FFPET CYP17  | Positive (≥ 1%) | E | 21/31 (67.7) | 3.7 (1.9 to 8.3) | – | – |
| AA | 16/24 (66.7) | 3.7 (1.9 to 8.3) | 0.47 | 1.28 (0.65 to 2.55) |
| AAE | 23/28 (82.1) | 6.5 (3.7 to 8.2) | 0.95 | 1.02 (0.56 to 1.86) |
| AA and AAE | 39/52 (75.0) | 3.9 (3.6 to 8.2) | 0.64 | 1.14 (0.66 to 1.95) |
| FFPET CYP19  | Positive (≥ 1%) | E | 45/60 (75.0) | 3.8 (3.5 to 5.5) | – | – |
|  |  | AA | 56/68 (82.4) | 3.7 (2.1 to 5.6) | 0.48 | 1.15 (0.77 to 1.72) |
|  |  | AAE | 51/62 (82.3) | 3.7 (3.6 to 6.8) | 0.74 | 1.07 (0.71 to 1.61) |
|  |  | AA and AAE | 107/130 (82.3) | 3.7 (3.5 to 5.5) | 0.50 | 1.13 (0.79 to 1.61) |

AR, androgen receptor; CI, confidence interval; CTC, circulating tumor cell; ER, estrogen receptor; FFPET, formalin-fixed paraffin-embedded tissue; HR, hazard ratio.

HR and *P* values are pairwise comparisons against E.

Only samples with ≥ 3 CTCs were evaluated. The sample sizes for CTC biomarkers differ due to failure of individual biomarker assays or lack of CTCs in individual samples.

**Supplementary Figure S1.** Comparison of associations of the negative expression of androgen receptor (AR) (< 10%) with progression-free survival (PFS). (A) circulating tumor cell (CTCs). (B) formalin-fixed paraffin-embedded tissues (FFPETs) by immunohistochemistry (IHC). (C) FFPETs collected < 1 year before first dose.





