**SUPPLEMENTAL TABLES**

**Table S1. Hazard Ratios from Multivariable Cox Proportional Hazards Regression Models Comparing High-risk Group with Node Negative Group (n=3424)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **IDFS** |  | **DRFS** |   |
| **Variables** | **HR (95% CI)** | **P-value** | **HR (95% CI)** | **P-value** |
| **High-risk** (ref: node negative) | 3.42 (2.69, 4.34) | <0.0001 | 3.46 (2.69, 4.44) | <0.0001 |
| Age at index, yrs. | 1.03 (1.02, 1.05) | <0.0001 | 1.04 (1.02, 1.05) | <0.0001 |
| **Race** (ref: white) |  |  |  |  |
|  Black | 1.42 (0.98, 2.06) | 0.0618 | 1.45 (0.98, 2.12) | 0.0604 |
|  Other race | 0.80 (0.57, 1.13) | 0.2066 | 0.76 (0.53, 1.09) | 0.1396 |
| **Menopausal status** (ref: peri/postmenopausal) |  |  |  |  |
|  Premenopausal | 1.66 (1.11, 2.48) | 0.0144 | 1.83 (1.20, 2.79) | 0.0050 |
|  NA - patient is male | 2.25 (0.97, 5.22) | 0.0588 | 2.01 (0.80, 5.06) | 0.1371 |
| **Surgical resection status** (ref: negative margins) |  |  |  |  |
|  Positive | 1.55 (1.03, 2.35) | 0.0376 | 1.58 (1.02, 2.43) | 0.0391 |
|  Not applicable | Not estimable |  | Not estimable |  |
| **Histology** (ref: invasive lobular carcinoma) |  |  |  |  |
|  Invasive ductal carcinoma | 0.80 (0.60, 1.07) | 0.1349 | 0.83 (0.61, 1.12) | 0.2230 |
| **PR status** (ref: PR negative) |  |  |  |  |
|  PR positive | 0.84 (0.58, 1.21) | 0.3461 | 0.80 (0.55, 1.16) | 0.2429 |
| **BRCA status** (ref: no mutation) |  |  |  |  |
|  BRCAmut | 0.75 (0.23, 2.48) | 0.6347 | 0.94 (0.28, 3.15) | 0.9154 |
| **ECOG PS** (ref: Score 0) |  |  |  |  |
|  Score 1 | 1.60 (1.11, 2.30) | 0.0117 | 1.75 (1.20, 2.56) | 0.0039 |
|  Score ≥2 | 2.22 (1.22, 4.03) | 0.0088 | 2.38 (1.30, 4.35) | 0.0050 |
| **Oncotype DX Breast Recurrence Score**(ref: <16) |  |  |  |  |
|  16-25 | 1.26 (0.63, 2.51) | 0.5131 | 1.38 (0.67, 2.88) | 0.3845 |
|  >25 | 3.40 (1.76, 6.58) | 0.0003 | 3.11 (1.50, 6.47) | 0.0023 |
| Abbreviations: BRCA=BReast CAncer gene; BRCAmut=BRCA mutation; CI=confidence interval; DRFS=distant relapse-free survival; ECOG=Eastern Cooperative Oncology Group; HR=hazard ratio; IDFS=invasive disease-free survival; NA=not applicable; PR=progesterone receptor; PS=performance score |

**Table S2. Hazard Ratios from Multivariable Cox Proportional Hazards Regression Models for US FDA-approved Indicated Patient Subgroup Compared with Non-high-risk Group (n=3607)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **IDFS** |  | **DRFS** |   |
| **Variables** | **HR (95% CI)** | **P-value** | **HR (95% CI)** | **P-value** |
| **High-risk subgroup**(ref: non-high-risk) | 3.29 (2.18, 4.94) | <.0001 | 3.34 (2.17, 5.15) | <.0001 |
| Age at index, yrs. | 1.05 (1.04, 1.07) | <.0001 | 1.06 (1.04, 1.08) | <.0001 |
| **Race** (ref: white) |  |  |  |  |
|  Black | 1.44 (0.96, 2.16) | 0.0806 | 1.49 (0.97, 2.28) | 0.0674 |
|  Other race | 0.86 (0.60, 1.22) | 0.3906 | 0.74 (0.50, 1.10) | 0.1315 |
| **Menopausal status** (ref: peri/postmenopausal) |  |  |  |  |
|  Premenopausal | 2.14 (1.33, 3.44) | 0.0018 | 2.16 (1.28, 3.64) | 0.0037 |
|  NA - patient is male | 1.36 (0.43, 4.30) | 0.6035 | 0.98 (0.24, 4.00) | 0.9799 |
| **Surgical resection status** (ref: negative margins) |  |  |  |  |
|  Positive | 1.06 (0.62, 1.80) | 0.8318 | 1.08 (0.62, 1.88) | 0.7736 |
| **Histology** (ref: invasive lobular carcinoma) |  |  |  |  |
|  Invasive ductal carcinoma | 0.72 (0.53, 0.99) | 0.0421 | 0.78 (0.55, 1.09) | 0.1466 |
| **PR status** (ref: PR negative) |  |  |  |  |
|  PR positive | 1.00 (0.67, 1.49) | 0.9844 | 0.90 (0.60, 1.36) | 0.6253 |
| **BRCA status** (ref: no mutation) |  |  |  |  |
|  BRCAmut | 0.72 (0.10, 5.34) | 0.7477 | 1.11 (0.15, 8.37) | 0.9187 |
| **ECOG PS** (ref: Score 0) |  |  |  |  |
|  Score 1 | 1.54 (1.02, 2.32) | 0.0410 | 1.65 (1.08, 2.54) | 0.0215 |
|  Score ≥2 | 3.89 (2.16, 7.00) | <.0001 | 4.26 (2.34, 7.73) | <.0001 |
| **Oncotype DX Breast Recurrence Score** (ref: <16) |  |  |  |  |
|  16-25 | 1.68 (0.88, 3.21) | 0.1189 | 1.64 (0.82, 3.26) | 0.1592 |
|  >25 | 3.56 (1.77, 7.17) | 0.0004 | 2.97 (1.38, 6.38) | 0.0053 |

Abbreviations: BRCA=BReast CAncer gene; BRCAmut=BRCA mutation; CI=confidence interval; DRFS=distant release-free survival; ECOG=Eastern Cooperative Oncology Group; FDA=Food and Drug Administration; HR=hazard ratio; IDFS=invasive disease-free survival; NA=not applicable; PR=progesterone receptor; PS=performance score; US=United States

**Table S3. Hazard Ratios for IDFS from Two Independent Cox Proportional Hazards Regression Models for Two Different Time Periods (High-risk vs. Non-high-risk is Comparison of Interest)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | **Event time shorter than 3.5 years****(n=4028)** |  | **Event time longer than 3.5 years****(n=1846)** |  |
| **Variables**  | **HR (95% CI)** | **P-value** | **HR (95% CI)** | **P-value** |
| **High-risk** (ref: non-high-risk) | 3.35 (2.52, 4.45) | <0.0001 | 2.66 (1.84, 3.84) | <0.0001 |
| Age at index, yrs. | 1.02 (1.01, 1.04) | 0.0032 | 1.06 (1.03, 1.08) | <0.0001 |
| **Race** (ref: white) |  |  |  |  |
|  Black | 1.41 (0.90, 2.19) | 0.1333 | 1.66 (1.00, 2.76) | 0.0499 |
|  Other race | 0.97 (0.66, 1.42) | 0.8708 | 0.60 (0.36, 1.02) | 0.0592 |
| **Menopausal status** (ref: peri/postmenopausal) |  |  |  |  |
|  Premenopausal | 1.40 (0.86, 2.27) | 0.1762 | 1.80 (1.01, 3.22) | 0.0480 |
|  NA - patient is male | 2.80 (1.11, 7.10) | 0.0296 | 1.34 (0.32, 5.63) | 0.6902 |
| **Surgical resection status** (ref: negative margins) |  |  |  |  |
|  Positive | 1.23 (0.74, 2.06) | 0.4280 | 1.61 (0.87, 2.95) | 0.1274 |
|  Not applicable | Not estimable |  | Not estimable |  |
| **Histology** (ref: invasive lobular carcinoma) |  |  |  |  |
|  Invasive ductal carcinoma | 0.88 (0.62, 1.26) | 0.4891 | 0.71 (0.48, 1.07) | 0.0983 |
| **PR status** (ref: PR negative) |  |  |  |  |
|  PR positive | 0.77 (0.51, 1.15) | 0.2021 | 1.20 (0.66, 2.19) | 0.5582 |
| **BRCA status** (ref: no mutation) |  |  |  |  |
|  BRCAmut | 1.05 (0.31, 3.56) | 0.9385 | 0.00 (0.00, 0.00) | 0.9778 |
| **ECOG PS** (ref: Score 0) |  |  |  |  |
|  Score 1 | 1.59 (1.04, 2.42) | 0.0306 | 1.25 (0.72, 2.18) | 0.4207 |
|  Score ≥2 | 3.03 (1.66, 5.50) | 0.0003 | 1.99 (0.84, 4.70) | 0.1164 |
| **Oncotype DX Breast Recurrence Score**(ref: < 16) |  |  |  |  |
|  16-25 | 1.61 (0.62, 4.18) | 0.3316 | 1.61 (0.71, 3.62) | 0.2530 |
|  >25 | 3.83 (1.46, 10.05) | 0.0063 | 3.48 (1.52, 7.97) | 0.0031 |

Abbreviations: BRCA=BReast CAncer gene; BRCAmut=BRCA mutation; CI=confidence interval; ECOG=Eastern Cooperative Oncology Group; HR=hazard ratio; IDFS=invasive disease-free survival; NA=not applicable; PR=progesterone receptor; PS=performance score

**Table S4. Hazard Ratios for IDFS from Two Independent Cox Proportional Hazards Regression Models for Two Different Time Periods (High-risk vs. Non-high-risk is Comparison of Interest)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Event time shorter than 3.5 years****(n=3424)** |  | **Event time longer than 3.5 years****(n=1574)** |  |
| **Variables**  | **HR (95% CI)** | **P-value** | **HR (95% CI)** | **P-value** |
| **High-risk** (ref: node negative) | 3.63 (2.68, 4.93) | <0.0001 | 3.01 (2.04, 4.46) | <0.0001 |
| Age at index, yrs. | 1.02 (1.00, 1.04) | 0.0497 | 1.06 (1.03, 1.08) | <0.0001 |
| **Race** (ref: white) |  |  |  |  |
|  Black | 1.39 (0.85, 2.26) | 0.1899 | 1.47 (0.83, 2.61) | 0.1886 |
|  Other race | 0.92 (0.60, 1.40) | 0.6915 | 0.65 (0.37, 1.15) | 0.1402 |
| **Menopausal status** (ref: peri/postmenopausal) |  |  |  |  |
|  Premenopausal | 1.38 (0.82, 2.33) | 0.2285 | 2.08 (1.11, 3.91) | 0.0223 |
|  NA - patient is male | 2.78 (0.98, 7.89) | 0.0553 | 1.55 (0.37, 6.59) | 0.5496 |
| **Surgical resection status** (ref: negative margins) |  |  |  |  |
|  Positive | 1.51 (0.90, 2.55) | 0.1205 | 1.61 (0.80, 3.24) | 0.1825 |
|  Not applicable | Not estimable |  | Not estimable |  |
| **Histology** (ref: invasive lobular carcinoma) |  |  |  |  |
|  Invasive ductal carcinoma | 0.87 (0.59, 1.27) | 0.4691 | 0.74 (0.47, 1.15) | 0.1796 |
| **PR status** (ref: PR negative) |  |  |  |  |
|  PR positive | 0.69 (0.45, 1.06) | 0.0937 | 1.23 (0.61, 2.46) | 0.5682 |
| **BRCA status** (ref: no mutation) |  |  |  |  |
|  BRCAmut | 1.06 (0.31, 3.66) | 0.9267 | Not estimable |  |
| **ECOG PS** (ref: Score 0) |  |  |  |  |
|  Score 1 | 1.79 (1.14, 2.82) | 0.0120 | 1.26 (0.68, 2.35) | 0.4636 |
|  Score ≥2 | 2.22 (1.02, 4.83) | 0.0459 | 2.09 (0.81, 5.35) | 0.1262 |
| **OncoType DX Breast Recurrence Score**(ref: < 16) |  |  |  |  |
|  16-25 | 1.56 (0.52, 4.65) | 0.4288 | 1.20 (0.48, 2.96) | 0.6974 |
|  >25 | 4.33 (1.52, 12.34) | 0.0061 | 3.14 (1.31, 7.48) | 0.0101 |

Abbreviation: BRCA=BReast CAncer gene; BRCAmut=BRCA mutation; CI=confidence interval; ECOG=Eastern Cooperative Oncology Group; HR=hazard ratio; IDFS=invasive disease-free survival; NA=not applicable; PR=progesterone receptor; PS=performance score