

Table S4. Unadjusted Cox regression analyses of patient and tumor characteristics at baseline

| | PFS | | OS | |
|--|------------------|-----------------|------------------|-----------------|
| | HR (95% CI) | <i>P</i> -value | HR (95% CI) | <i>P</i> -value |
| Age at diagnosis MBC (years) | | | | |
| <65 | 1.00 | | 1.00 | |
| ≥65 | 0.82 (0.57-1.17) | 0.27 | 1.12 (0.73-1.73) | 0.60 |
| ECOG | | | | |
| 0 | 1.00 | | 1.00 | |
| 1 | 1.27 (0.83-1.95) | 0.27 | 1.68 (0.99-2.85) | 0.05 |
| 2 | 1.34 (0.79-2.28) | 0.28 | 2.67 (1.49-4.78) | 0.001 |
| NHG | | | | |
| I-II | 1.00 | | 1.00 | |
| III | 1.37 (0.90-2.07) | 0.14 | 1.37 (0.83-2.25) | 0.22 |
| PT Tumor size (mm) | | | | |
| ≤20 (T1) | 1.00 | | 1.00 | |
| >20 (T2-4) | 0.93 (0.63-1.36) | 0.70 | 1.07 (0.68-1.70) | 0.76 |
| PT Node status | | | | |
| Negative | 1.00 | | 1.00 | |
| Positive | 1.02 (0.63-1.65) | 0.94 | 0.98 (0.65-1.48) | 0.94 |
| Subtype | | | | |
| HR+HER2- | 1.00 | | 1.00 | |
| HER2+ | 0.76 (0.43-1.32) | 0.33 | 0.72 (0.34-1.52) | 0.39 |
| HR-HER2- | 2.58 (1.58-4.20) | <0.001 | 5.42 (3.08-9.55) | <0.001 |
| Metastasis-free interval (years) | | | | |
| 0 | 0.51 (0.29-0.92) | 0.02 | 0.27 (0.14-0.55) | <0.001 |
| >0-3 | 1.00 | | 1.00 | |
| >3 | 0.65 (0.40-1.04) | 0.07 | 0.46 (0.27-0.77) | 0.003 |
| No metastatic sites | | | | |
| <3 | 1.00 | | 1.00 | |
| ≥3 | 2.07 (1.41-3.03) | <0.001 | 2.18 (1.41-3.37) | <0.001 |
| Site of metastasis | | | | |
| Non-visceral | 1.00 | | 1.00 | |
| Visceral | 1.69 (1.16-2.45) | 0.006 | 1.59 (1.02-2.48) | 0.04 |
| Baseline CA15-3 (kE/L) | | | | |
| <30 | 1.00 | | 1.00 | |
| ≥30 | 1.40 (0.86-2.29) | 0.17 | 1.56 (0.86-2.85) | 0.15 |
| 1st line treatment for MBC | | | | |

| | | | | |
|---------------|------------------|------|------------------|-------|
| Endocrine | 1.00 | | 1.00 | |
| Chemotherapy | 1.65 (1.10-2.47) | 0.02 | 2.07 (1.25-3.42) | 0.005 |
| HER2-targeted | 0.82 (0.42-1.61) | 0.56 | 0.91 (0.37-2.23) | 0.83 |

Abbreviations: PFS, progression-free survival; OS, overall survival; HR, hazard ratio; MBC, metastatic breast cancer; NHG, Nottingham histological grade; PT, primary tumor; HR, hormone receptor; HER2, human epidermal growth factor receptor 2