|  |
| --- |
| **Supplementary Table S1:** Hazard Ratios (95% CI) and chi-square values for all recurrence and all individual genes and gene modules according to time periods in all patients, HER2-ve patients, and HER2-ve/Node-ve patients. |
|  |  |  |  |  |  |  |  |
|  |  |  | **All patients (N=1125)** |  |  |  |  |
|  | **0-10 years** |  | **0-5 years** |  | **5-10 years** |  |  |
|  | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **P-hetero** |
| **HER2 genes** |  |  |  |  |  |  |  |
| GRB7 | 1.04 (0.89-1.21) | 0.25 | 1.12 (0.91-1.38) | 1.04 | 0.93 (0.74-1.17) | 0.38 | 0.3 |
| HER2 | 1.11 (0.97-1.28) | 2.33 | 1.11 (0.91-1.36) | 1.07 | 1.09 (0.89-1.32) | 0.67 | 0.9 |
| **HER module** | 1.05 (0.90-1.22) | 0.38 | 1.12 (0.91-1.38) | 1.07 | 0.95 (0.76-1.19) | 0.22 | 0.3 |
| **HER module (with threshold)** | 1.29 (1.06-1.56) | 5.54 | 1.41 (1.10-1.82) | 5.78 | 1.15 (0.84-1.57) | 0.7 |   |
| **Proliferation genes** |  |  |  |  |  |  |
| Cyclin B1 | 1.82 (1.51-2.20) | 39.4 | 1.80 (1.36-2.37) | 17.3 | 1.78 (1.37-2.32) | 18.4 | 0.9 |
| Ki-67 | 1.64 (1.42-1.89) | 49.2 | 1.62 (1.31-2.01) | 20.7 | 1.59 (1.31-1.94) | 23.2 | 0.9 |
| MYLB2 | 1.52 (1.37-1.70) | 56 | 1.65 (1.40-1.94) | 35.5 | 1.43 (1.23-1.66) | 20.4 | 0.2 |
| STK15 | 1.88 (1.58-2.23) | 45.4 | 1.96 (1.52-2.54) | 23.5 | 1.75 (1.37-2.23) | 17.9 | 0.5 |
| Survivin | 1.44 (1.29-1.60) | 42.3 | 1.51 (1.28-1.78) | 24.6 | 1.37 (1.18-1.60) | 16.8 | 0.4 |
| **Proliferation module** | 1.89 (1.61-2.21) | 61.3 | 2.00 (1.57-2.55) | 32.5 | 1.76 (1.41-2.20) | 25.2 | 0.4 |
| **Proliferation module (with threshold)** | 2.88 (1.97-4.21) | 23.6 | 3.35 (1.99-5.66) | 15.7 | 2.55 (1.45-4.48) | 8.49 |   |
| **Estrogen genes** |  |  |  |  |  |  |  |
| BCL2 | 0.62 (0.54-0.72) | 41.3 | 0.59 (0.48-0.72) | 24.9 | 0.67 (0.54-0.81) | 15.4 | 0.4 |
| SCUBE2 | 0.91 (0.85-0.99) | 5.1 | 0.80 (0.71-0.89) | 16.3 | 1.05 (0.93-1.17) | 0.61 | 0.001 |
| ER | 0.97 (0.87-1.09) | 0.26 | 0.82 (0.71-0.95) | 6.27 | 1.14 (0.96-1.34) | 2.4 | 0.004 |
| PgR | 0.92 (0.86-0.98) | 6.08 | 0.84 (0.76-0.93) | 12 | 0.99 (0.90-1.09) | 0.05 | 0.02 |
| **Estrogen module** | 0.79 (0.70-0.89) | 14.1 | 0.64 (0.54-0.75) | 25.9 | 0.97 (0.81-1.16) | 0.1 | 0.001 |
| **Invasion genes** |  |  |  |  |  |  |  |
| Cathepsin L2 | 1.27 (1.10-1.48) | 10 | 1.20 (0.96-1.50) | 2.64 | 1.31 (1.06-1.61) | 6.39 | 0.6 |
| Stromelysin 3 | 1.26 (1.14-1.39) | 20.4 | 1.31 (1.12-1.53) | 15.3 | 1.23 (1.07-1.42) | 8.62 | 0.6 |
| **Invasion module** | 1.60 (1.35-1.90) | 30.4 | 1.64 (1.27-2.12) | 15 | 1.58 (1.24-2.01) | 14.8 | 0.8 |
| **Other genes** |  |  |  |  |  |  |  |
| BAG1 | 0.70 (0.58-0.85) | 14 | 0.54 (0.40-0.72) | 18.7 | 0.81 (0.63-1.06) | 2.42 | 0.04 |
| CD68 | 1.02 (0.82-1.29) | 0.04 | 1.07 (0.76-1.50) | 0.15 | 1.02 (0.74-1.41) | 0.02 | 0.9 |
| GSTM1 | 0.77 (0.69-0.86) | 20.9 | 0.70 (0.60-0.82) | 18.6 | 0.84 (0.72-0.98) | 4.62 | 0.1 |
| **Recurrence Score** | **1.028 (1.020-1.036)** | **39.2** | **1.036 (1.026-1.047)** | **37.8** | **1.018 (1.001-1.034)** | **6.8** | **0.03** |
|  |  |  |  |  |  |  |  |
|  |  |  | **HER2-ve (N=1009)** |  |  |  |  |
|  | **0-10 years** |  | **0-5 years** |  | **5-10 years** |  |  |
|  | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **P-hetero** |
| **HER2 genes** |  |  |  |  |  |  |  |
| GRB7 | 0.79 (0.64-0.97) | 4.91 | 0.71 (0.52-0.97) | 4.56 | 0.79 (0.59-1.06) | 2.49 | 0.6 |
| HER2 | 0.90 (0.73-1.11) | 0.94 | 0.70 (0.51-0.96) | 4.89 | 1.01 (0.75-1.36) | 0.01 | 0.09 |
| **HER module** | 0.79 (0.63-0.98) | 4.64 | 0.69 (0.50-0.95) | 4.87 | 0.80 (0.59-1.08) | 2.12 | 0.5 |
| **HER module (with threshold)** | 0.89 (0.50-1.60) | 0.15 | 0.44 (0.14-1.42) | 2.31 | 1.17 (0.58-2.38) | 0.19 |   |
| **Proliferation genes** |  |  |  |  |  |  |
| Cyclin B1 | 1.85 (1.51-2.26) | 35.5 | 1.81 (1.32-2.47) | 13.9 | 1.81 (1.37-2.39) | 18 | 0.9 |
| Ki-67 | 1.64 (1.40-1.91) | 42 | 1.52 (1.19-1.93) | 12.3 | 1.66 (1.35-2.04) | 24.6 | 0.6 |
| MYLB2 | 1.51 (1.34-1.70) | 44.9 | 1.59 (1.32-1.91) | 23.1 | 1.46 (1.24-1.71) | 20.5 | 0.5 |
| STK15 | 1.95 (1.61-2.36) | 40.9 | 2.02 (1.49-2.73) | 18.4 | 1.83 (1.41-2.39) | 18 | 0.6 |
| Survivin | 1.45 (1.29-1.64) | 37.7 | 1.50 (1.24-1.81) | 18.1 | 1.42 (1.21-1.66) | 18.2 | 0.6 |
| **Proliferation module** | 1.90 (1.60-2.27) | 53 | 1.94 (1.47-2.56) | 22.7 | 1.84 (1.45-2.33) | 26.1 | 0.8 |
| **Proliferation module (with threshold)** | 2.86 (1.84-4.43) | 17.1 | 3.18 (1.68-6.05) | 9.58 | 2.72 (1.46-5.06) | 7.85 |   |
| **Estrogen genes** |  |  |  |  |  |  |  |
| BCL2 | 0.61 (0.52-0.71) | 35.8 | 0.57 (0.45-0.73) | 19.9 | 0.64 (0.52-0.81) | 14.5 | 0.5 |
| SCUBE2 | 0.96 (0.88-1.04) | 0.94 | 0.84 (0.74-0.96) | 6.67 | 1.07 (0.94-1.20) | 1.1 | 0.009 |
| ER | 1.05 (0.92-1.20) | 0.51 | 0.88 (0.73-1.07) | 1.61 | 1.19 (0.99-1.43) | 3.54 | 0.03 |
| PgR | 0.94 (0.87-1.01) | 2.62 | 0.86 (0.76-0.96) | 6.87 | 1.00 (0.90-1.11) | 0 | 0.05 |
| **Estrogen module** | 0.83 (0.72-0.96) | 6.13 | 0.66 (0.54-0.81) | 14.4 | 1.01 (0.82-1.23) | 0 | 0.004 |
| **Invasion genes** |  |  |  |  |  |  |  |
| Cathepsin L2 | 1.26 (1.07-1.48) | 7.6 | 1.19 (0.93-1.54) | 1.84 | 1.27 (1.02-1.59) | 4.62 | 0.7 |
| Stromelysin 3 | 1.25 (1.12-1.39) | 16.4 | 1.30 (1.09-1.55) | 9.24 | 1.23 (1.06-1.42) | 7.71 | 0.6 |
| **Invasion module** | 1.56 (1.30-1.87) | 23.4 | 1.60 (1.20-2.14) | 10.7 | 1.53 (1.20-1.96) | 11.9 | 0.8 |
| **Other genes** |  |  |  |  |  |  |  |
| BAG1 | 0.73 (0.58-0.90) | 8.92 | 0.52 (0.36-0.73) | 14.8 | 0.85 (0.64-1.13) | 1.28 | 0.03 |
| CD68 | 1.03 (0.80-1.32) | 0.04 | 1.08 (0.73-1.60) | 0.15 | 1.03 (0.73-1.45) | 0.03 | 0.9 |
| GSTM1 | 0.77 (0.68-0.87) | 17.1 | 0.73 (0.61-0.87) | 11.3 | 0.80 (0.68-0.95) | 6.29 | 0.4 |
| **Recurrence Score** | **1.033 (1.022-1.045)** | **27** | **1.045 (1.028-1.062)** | **23.5** | **1.024 (1.007-1.042)** | **6.74** | **0.09** |
|  |  |  |  |  |  |  |  |
|  |  |  | **HER2-ve/Node-ve (N=751)** |  |  |  |  |
|  | **0-10 years** |  | **0-5 years** |  | **5-10 years** |  |  |
|  | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **P-hetero** |
| **HER2 genes** |  |  |  |  |  |  |  |
| GRB7 | 0.89 (0.66-1.18) | 0.7 | 0.66 (0.43-1.02) | 3.35 | 0.95 (0.64-1.39) | 0.08 | 0.07 |
| HER2 | 0.96 (0.71-1.28) | 0.09 | 0.60 (0.38-0.94) | 4.83 | 1.13 (0.76-1.68) | 0.38 | 0.07 |
| **HER module** | 0.89 (0.66-1.19) | 0.65 | 0.64 (0.41-1.00) | 3.69 | 0.96 (0.64-1.43) | 0.04 | 0.06 |
| **HER module (with threshold)** | 1.23 (0.61-2.50) | 0.33 | 0.10 (0.007-1.36) | 4.99 | 2.02 (0.94-4.35) | 2.68 |   |
| **Proliferation genes** |  |  |  |  |  |  |
| Cyclin B1 | 1.80 (1.37-2.36) | 18.1 | 1.66 (1.07-2.57) | 5.03 | 1.79 (1.25-2.57) | 9.95 | 0.6 |
| Ki-67 | 1.71 (1.39-2.11) | 27.8 | 1.56 (1.11-2.19) | 7.07 | 1.72 (1.31-2.26) | 16.4 | 0.5 |
| MYLB2 | 1.62 (1.38-1.89) | 34.4 | 1.69 (1.30-2.18) | 15.2 | 1.59 (1.29-1.95) | 18 | 0.8 |
| STK15 | 1.95 (1.52-2.50) | 24.4 | 1.99 (1.31-3.03) | 9.12 | 1.83 (1.31-2.55) | 11.1 | 0.8 |
| Survivin | 1.44 (1.23-1.69) | 18.7 | 1.48 (1.13-1.93) | 8.09 | 1.41 (1.14-1.74) | 10 | 0.9 |
| **Proliferation module** | 1.96 (1.56-2.48) | 32.8 | 1.95 (1.33-2.87) | 11.8 | 1.92 (1.41-2.60) | 17.3 | 0.9 |
| **Proliferation module (with threshold)** | 3.21 (1.83-5.63) | 12.4 | 3.84 (1.66-8.93) | 7.14 | 2.86 (1.29-6.35) | 5.13 |   |
| **Estrogen genes** |  |  |  |  |  |  |  |
| BCL2 | 0.59 (0.47-0.74) | 20.4 | 0.49 (0.34-0.69) | 15.2 | 0.68 (0.50-0.92) | 6.1 | 0.08 |
| SCUBE2 | 0.89 (0.80-1.00) | 3.83 | 0.76 (0.63-0.90) | 9.08 | 1.03 (0.88-1.20) | 0.11 | 0.01 |
| ER | 1.03 (0.87-1.23) | 0.12 | 0.81 (0.62-1.05) | 2.5 | 1.20 (0.95-1.51) | 2.28 | 0.05 |
| PgR | 0.92 (0.83-1.02) | 2.28 | 0.91 (0.77-1.07) | 1.35 | 0.93 (0.81-1.07) | 1.02 | 0.6 |
| **Estrogen module** | 0.78 (0.64-0.94) | 6.54 | 0.63 (0.47-0.83) | 9.51 | 0.92 (0.71-1.20) | 0.39 | 0.03 |
| **Invasion genes** |  |  |  |  |  |  |  |
| Cathepsin L2 | 1.18 (0.95-1.47) | 2.27 | 1.13 (0.79-1.63) | 0.47 | 1.14 (0.86-1.52) | 0.79 | 0.7 |
| Stromelysin 3 | 1.16 (1.01-1.34) | 4.29 | 1.29 (1.01-1.64) | 4.41 | 1.13 (0.94-1.36) | 1.63 | 0.4 |
| **Invasion module** | 1.37 (1.07-1.74) | 6.56 | 1.56 (1.03-2.35) | 4.67 | 1.28 (0.93-1.76) | 2.41 | 0.6 |
| **Other genes** |  |  |  |  |  |  |  |
| BAG1 | 0.74 (0.55-0.99) | 4.21 | 0.42 (0.25-0.71) | 11.5 | 0.91 (0.63-1.32) | 0.24 | 0.06 |
| CD68 | 1.07 (0.76-1.51) | 0.13 | 1.21 (0.69-2.12) | 0.44 | 1.02 (0.64-1.61) | 0 | 0.3 |
| GSTM1 | 0.76 (0.64-0.89) | 10.3 | 0.64 (0.50-0.83) | 10.7 | 0.85 (0.68-1.08) | 1.75 | 0.1 |
| **Recurrence Score** | **1.037 (1.022-1.052)** | **20** | **1.049 (1.027-1.072)** | **15.1** | **1.028 (1.007-1.051)** | **5.71** | **0.2** |
|  |  |  |  |  |  |  |  |

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| **Supplementary Table S2:** Hazard Ratios (95% CI) and chi-square values for distant recurrence and all individual genes and gene modules according to time periods in all patients, HER2-ve patients, and HER2-ve/Node-ve patients. |
|  |  |  |  |  |  |  |  |
|  |  |  | **All patients (N=1125)** |  |  |  |  |
|  | **0-10 years** |  | **0-5 years** |  | **5-10 years** |  |  |
|  | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **P-hetero** |
| **HER2 genes** |  |  |  |  |  |  |  |
| GRB7 | 1.07 (0.90-1.27) | 0.62 | 1.13 (0.90-1.43) | 1.08 | 1.01 (0.78-1.29) | 1E-04 | 0.5 |
| HER2 | 1.16 (0.99-1.35) | 3.37 | 1.15 (0.92-1.42) | 1.46 | 1.17 (0.94-1.45) | 1.93 | 0.9 |
| **HER module** | 1.08 (0.91-1.29) | 0.84 | 1.14 (0.90-1.44) | 1.16 | 1.03 (0.80-1.32) | 0.04 | 0.5 |
| **HER module (with threshold)** | 1.36 (1.11-1.67) | 7.06 | 1.44 (1.10-1.89) | 5.37 | 1.28 (0.94-1.74) | 2.01 |   |
| **Proliferation genes** |  |  |  |  |  |  |
| Cyclin B1 | 2.28 (1.83-2.84) | 54.5 | 2.17 (1.59-2.97) | 24.1 | 2.39 (1.75-3.27) | 30.58 | 0.7 |
| Ki-67 | 1.82 (1.53-2.16) | 51 | 1.84 (1.43-2.35) | 25.4 | 1.80 (1.42-2.28) | 25.61 | 0.9 |
| MYLB2 | 1.63 (1.43-1.85) | 55.2 | 1.74 (1.45-2.09) | 35.1 | 1.53 (1.28-1.82) | 21.08 | 0.3 |
| STK15 | 1.96 (1.62-2.39) | 40 | 1.96 (1.47-2.60) | 18.9 | 1.97 (1.51-2.58) | 21.16 | 0.9 |
| Survivin | 1.55 (1.37-1.77) | 46 | 1.60 (1.33-1.93) | 25.5 | 1.51 (1.27-1.80) | 20.77 | 0.7 |
| **Proliferation module** | 2.15 (1.78-2.60) | 64.9 | 2.23 (1.70-2.93) | 34.6 | 2.08 (1.60-2.70) | 30.44 | 0.7 |
| **Proliferation module (with threshold)** | 3.52 (2.34-5.31) | 27.3 | 3.50 (1.96-6.22) | 13.8 | 3.55 (1.98-6.37) | 13.54 |   |
| **Estrogen genes** |  |  |  |  |  |  |  |
| BCL2 | 0.62 (0.53-0.73) | 32 | 0.60 (0.48-0.75) | 18.5 | 0.64 (0.51-0.81) | 13.68 | 0.7 |
| SCUBE2 | 0.90 (0.82-0.98) | 5.56 | 0.78 (0.69-0.88) | 15.1 | 1.04 (0.91-1.19) | 0.39 | 0.002 |
| ER | 0.99 (0.88-1.14) | 0 | 0.85 (0.72-1.01) | 3.19 | 1.20 (0.98-1.46) | 3.37 | 0.01 |
| PgR | 0.90 (0.83-0.97) | 6.63 | 0.83 (0.74-0.92) | 11.5 | 0.99 (0.88-1.11) | 0.05 | 0.03 |
| **Estrogen module** | 0.77 (0.67-0.89) | 12.8 | 0.63 (0.53-0.76) | 21.9 | 0.97 (0.79-1.20) | 0.07 | 0.003 |
| **Invasion genes** |  |  |  |  |  |  |  |
| Cathepsin L2 | 1.34 (1.13-1.59) | 11 | 1.34 (1.05-1.71) | 5.35 | 1.34 (1.06-1.71) | 5.62 | 0.9 |
| Stromelysin 3 | 1.25 (1.11-1.41) | 14.4 | 1.30 (1.09-1.54) | 9.34 | 1.21 (1.03-1.43) | 5.38 | 0.6 |
| **Invasion module** | 1.65 (1.35-2.02) | 25.1 | 1.74 (1.30-2.33) | 14.8 | 1.57 (1.19-2.08) | 10.55 | 0.6 |
| **Other genes** |  |  |  |  |  |  |  |
| BAG1 | 0.66 (0.53-0.83) | 13.5 | 0.55 (0.40-0.76) | 13.9 | 0.80 (0.58-1.09) | 2.14 | 0.1 |
| CD68 | 0.98 (0.75-1.28) | 0.03 | 0.97 (0.67-1.42) | 0.02 | 0.98 (0.68-1.43) | 0.01 | 0.9 |
| GSTM1 | 0.76 (0.67-0.86) | 17.5 | 0.72 (0.60-0.85) | 13.1 | 0.81 (0.67-0.97) | 5.19 | 0.4 |
| **Recurrence Score** | **1.030 (1.021-1.046)** | **38.5** | **1.036 (1.025-1.048)** | **31.8** | **1.022 (1.009-1.036)** | **9.23** | **0.1** |
|  |  |  |  |  |  |  |  |
|  |  |  | **HER2-ve (N=1009)** |  |  |  |  |
|  | **0-10 years** |  | **0-5 years** |  | **5-10 years** |  |  |
|  | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **P-hetero** |
| **HER2 genes** |  |  |  |  |  |  |  |
| GRB7 | 0.72 (0.56-0.92) | 6.68 | 0.72 (0.50-1.02) | 3.24 | 0.72 (0.51-1.02) | 3.43 | 0.9 |
| HER2 | 0.82 (0.63-1.05) | 2.42 | 0.72 (0.50-1.03) | 3.12 | 0.92 (0.65-1.30) | 0.22 | 0.3 |
| **HER module** | 0.71 (0.55-0.92) | 6.53 | 0.70 (0.48-1.02) | 3.43 | 0.72 (0.50-1.04) | 3.12 | 0.9 |
| **HER module (with threshold)** | 0.82 (0.40-1.68) | 0.32 | 0.71 (0.23-2.21) | 0.37 | 0.90 (0.35-2.30) | 0.05 |   |
| **Proliferation genes** |  |  |  |  |  |  |
| Cyclin B1 | 2.46 (1.92-3.14) | 52.6 | 2.41 (1.68-3.46) | 23.3 | 2.49 (1.78-3.49) | 29.32 | 0.9 |
| Ki-67 | 1.84 (1.52-2.23) | 43 | 1.77 (1.34-2.35) | 16.9 | 1.90 (1.47-2.46) | 26.17 | 0.7 |
| MYLB2 | 1.62 (1.40-1.86) | 42.5 | 1.71 (1.38-2.10) | 24 | 1.54 (1.27-1.87) | 18.94 | 0.5 |
| STK15 | 2.09 (1.67-2.61) | 36 | 2.12 (1.51-2.96) | 16.7 | 2.06 (1.53-2.79) | 19.36 | 0.9 |
| Survivin | 1.60 (1.39-1.85) | 41.1 | 1.63 (1.31-2.02) | 19.9 | 1.58 (1.30-1.91) | 21.22 | 0.8 |
| **Proliferation module** | 2.24 (1.81-2.77) | 56.3 | 2.28 (1.66-3.14) | 26.7 | 2.20 (1.65-2.93) | 29.62 | 0.9 |
| **Proliferation module (with threshold)** | 3.78 (2.34-6.11) | 21.9 | 3.57 (1.77-7.22) | 9.43 | 3.98 (2.07-7.67) | 12.56 |   |
| **Estrogen genes** |  |  |  |  |  |  |  |
| BCL2 | 0.61 (0.50-0.74) | 24.4 | 0.58 (0.44-0.76) | 14.3 | 0.64 (0.49-0.84) | 10.38 | 0.6 |
| SCUBE2 | 0.96 (0.86-1.06) | 0.63 | 0.84 (0.72-0.97) | 5.65 | 1.09 (0.94-1.26) | 1.38 | 0.01 |
| ER | 1.14 (0.97-1.33) | 2.5 | 0.96 (0.77-1.21) | 0.1 | 1.32 (1.06-1.65) | 6.15 | 0.05 |
| PgR | 0.94 (0.86-1.03) | 1.86 | 0.84 (0.74-0.95) | 6.9 | 1.04 (0.92-1.18) | 0.38 | 0.02 |
| **Estrogen module** | 0.85 (0.72-1.00) | 3.39 | 0.66 (0.52-0.84) | 11.2 | 1.09 (0.85-1.40) | 0.49 | 0.004 |
| **Invasion genes** |  |  |  |  |  |  |  |
| Cathepsin L2 | 1.30 (1.07-1.58) | 6.8 | 1.34 (1.00-1.79) | 3.9 | 1.26 (0.97-1.65) | 2.99 | 0.8 |
| Stromelysin 3 | 1.22 (1.07-1.40) | 9.45 | 1.27 (1.04-1.55) | 6.04 | 1.18 (0.99-1.41) | 3.7 | 0.6 |
| **Invasion module** | 1.55 (1.24-1.93) | 15.8 | 1.68 (1.20-2.34) | 9.79 | 1.45 (1.08-1.95) | 6.4 | 0.5 |
| **Other genes** |  |  |  |  |  |  |  |
| BAG1 | 0.73 (0.56-0.94) | 6.14 | 0.56 (0.38-0.83) | 8.78 | 0.89 (0.64-1.26) | 0.43 | 0.08 |
| CD68 | 0.98 (0.73-1.33) | 0.02 | 1.02 (0.65-1.59) | 0.01 | 0.95 (0.63-1.43) | 0.06 | 0.8 |
| GSTM1 | 0.76 (0.65-0.87) | 13.6 | 0.73 (0.59-0.90) | 8.15 | 0.78 (0.64-0.95) | 5.64 | 0.7 |
| **Recurrence Score** | **1.037 (1.023-1.051)** | **23.6** | **1.047 (1.028-1.067)** | **20.7** | **1.026 (1.004-1.047)** | **5.27** | **0.1** |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  | **HER2-ve/Node-ve (N=751)** |  |  |  |  |
|  | **0-10 years** |  | **0-5 years** |  | **5-10 years** |  |  |
|  | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **P-hetero** |
| **HER2 genes** |  |  |  |  |  |  |  |
| GRB7 | 0.74 (0.51-1.07) | 2.59 | 0.66 (0.38-1.15) | 2.02 | 0.80 (0.49-1.30) | 0.82 | 0.3 |
| HER2 | 0.80 (0.55-1.16) | 1.41 | 0.55 (0.31-0.97) | 4.09 | 1.03 (0.63-1.69) | 0.02 | 0.2 |
| **HER module** | 0.73 (0.50-1.07) | 2.61 | 0.63 (0.36-1.12) | 2.32 | 0.81 (0.49-1.34) | 0.69 | 0.6 |
| **HER module (with threshold)** | 0.99 (0.36-2.67) | 0 | 0.29 (0.03-3.42) | 1.29 | 1.51 (0.52-4.40) | 0.5 |   |
| **Proliferation genes** |  |  |  |  |  |  |
| Cyclin B1 | 2.74 (1.92-3.91) | 31.1 | 3.08 (1.75-5.42) | 15.4 | 2.53 (1.60-4.00) | 16 | 0.7 |
| Ki-67 | 2.19 (1.65-2.90) | 32.3 | 2.19 (1.38-3.48) | 12.2 | 2.18 (1.53-3.11) | 20.11 | 0.8 |
| MYLB2 | 1.88 (1.53-2.30) | 35.5 | 2.08 (1.50-2.88) | 18.6 | 1.76 (1.36-2.29) | 17.5 | 0.4 |
| STK15 | 2.20 (1.61-3.01) | 20.6 | 2.41 (1.45-3.99) | 9.77 | 2.09 (1.40-3.12) | 11.03 | 0.7 |
| Survivin | 1.71 (1.38-2.11) | 24.6 | 1.73 (1.22-2.46) | 9.71 | 1.69 (1.30-2.21) | 14.93 | 0.9 |
| **Proliferation module** | 2.62 (1.92-3.57) | 38.2 | 2.86 (1.72-4.75) | 17.2 | 2.48 (1.68-3.68) | 21.15 | 0.8 |
| **Proliferation module (with threshold)** | 4.85 (2.56-9.19) | 16.5 | 5.01 (1.87-13.42) | 7.17 | 4.74 (2.05-10.97) | 9.28 |   |
| **Estrogen genes** |  |  |  |  |  |  |  |
| BCL2 | 0.55 (0.41-0.73) | 15.9 | 0.48 (0.30-0.75) | 9.61 | 0.60 (0.41-0.88) | 6.81 | 0.3 |
| SCUBE2 | 0.90 (0.78-1.05) | 1.76 | 0.72 (0.58-0.91) | 7.59 | 1.06 (0.87-1.29) | 0.3 | 0.009 |
| ER | 1.15 (0.91-1.44) | 1.39 | 0.90 (0.64-1.27) | 0.34 | 1.36 (1.00-1.84) | 4.04 | 0.1 |
| PgR | 0.96 (0.84-1.10) | 0.29 | 0.91 (0.74-1.13) | 0.65 | 0.99 (0.84-1.19) | 0.001 | 0.4 |
| **Estrogen module** | 0.83 (0.65-1.06) | 2.12 | 0.63 (0.44-0.90) | 5.67 | 1.02 (0.73-1.43) | 0.01 | 0.04 |
| **Invasion genes** |  |  |  |  |  |  |  |
| Cathepsin L2 | 1.23 (0.93-1.64) | 2.1 | 1.52 (0.97-2.38) | 3.28 | 1.08 (0.75-1.56) | 0.17 | 0.3 |
| Stromelysin 3 | 1.19 (0.98-1.43) | 3.27 | 1.24 (0.91-1.69) | 1.95 | 1.15 (0.91-1.46) | 1.45 | 0.8 |
| **Invasion module** | 1.45 (1.05-2.00) | 5.4 | 1.80 (1.05-3.09) | 4.86 | 1.28 (0.86-1.91) | 1.54 | 0.4 |
| **Other genes** |  |  |  |  |  |  |  |
| BAG1 | 0.79 (0.54-1.15) | 1.59 | 0.49 (0.26-0.95) | 4.79 | 1.02 (0.65-1.61) | 0.01 | 0.2 |
| CD68 | 1.10 (0.71-1.73) | 0.19 | 1.23 (0.60-2.51) | 0.31 | 1.04 (0.59-1.83) | 0.01 | 0.3 |
| GSTM1 | 0.70 (0.57-0.87) | 10.2 | 0.59 (0.43-0.81) | 9.55 | 0.79 (0.60-1.05) | 2.5 | 0.2 |
| **Recurrence Score** | **1.042 (1.023-1.062)** | **15.6** | **1.056 (1.028-1.084)** | **12.5** | **1.032 (1.005-1.059)** | **4.65** | **0.3** |

|  |
| --- |
| **Supplementary Table S3:** Comparison of GHI and IHC genes according to time period in all patients, HER2-ve, and HER2-ve/Node-ve patients. |
|  |  |  |  |  |  |  |
|  |  |  | **All patients** |  |  |  |
|  | **0-10 years** |  | **0-5 years** |  | **5-10 years** |  |
|   | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** |
| **GHI** |  |  |  |  |  |  |
| ER | 0.96 (0.81-1.14) | 0.26 | 0.74 (0.59-0.93) | 6.27 | 1.22 (0.95-1.57) | 2.4 |
| PgR | 0.78 (0.64-0.95) | 6.08 | 0.60 (0.46-0.80) | 11.99 | 0.97 (0.73-1.28) | 0.05 |
| **IHC** |  |  |  |  |  |  |
| ERH10 | 0.76 (0.66-0.88) | 12.91 | 0.69 (0.56-0.84) | 12.17 | 0.87 (0.70-1.07) | 1.65 |
| PGR10 | 0.59 (0.46-0.76) | 16.12 | 0.43 (0.29-0.63) | 18.81 | 0.80 (0.56-1.15) | 1.45 |
|  |  |  | **HER2-ve** |  |  |  |
|  | **0-10 years** |  | **0-5 years** |  | **5-10 years** |  |
|  | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** |
| **GHI** |  |  |  |  |  |  |
| ER | 1.08 (0.88-1.32) | 0.51 | 0.82 (0.61-1.11) | 1.61 | 1.31 (0.99-1.73) | 3.54 |
| PgR | 0.83 (0.67-1.04) | 2.62 | 0.64 (0.46-0.89) | 6.87 | 1.01 (0.74-1.37) | 0.001 |
| **IHC** |  |  |  |  |  |  |
| ERH10 | 0.81 (0.69-0.95) | 5.96 | 0.77 (0.60-0.99) | 3.78 | 0.87 (0.69-1.10) | 1.35 |
| PGR10 | 0.63 (0.47-0.83) | 10.57 | 0.47 (0.30-0.73) | 11.46 | 0.81 (0.55-1.18) | 1.18 |
|  |  |  | **HER2-ve/Node-ve** |  |  |  |
|  | **0-10 years** |  | **0-5 years** |  | **5-10 years** |  |
|  | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** | **HR (95% CI)** | **LR-χ2** |
| **GHI** |  |  |  |  |  |  |
| ER | 1.05 (0.79-1.38) | 0.12 | 0.72 (0.47-1.11) | 2.5 | 1.27 (0.88-1.84) | 2.28 |
| PgR | 0.78 (0.57-1.06) | 2.28 | 0.71 (0.42-1.18) | 1.35 | 0.85 (0.57-1.27) | 1.02 |
| **IHC** |  |  |  |  |  |  |
| ERH10 | 0.72 (0.58-0.89) | 8.25 | 0.68 (0.48-0.97) | 4.02 | 0.75 (0.56-1.00) | 3.52 |
| PGR10 | 0.56 (0.38-0.82) | 8.63 | 0.42 (0.22-0.81) | 6.58 | 0.72 (0.43-1.19) | 1.63 |
| All HRs are adjusted for a difference between the 25th and 75th percentile. |  |  |