**Supplementary Table S1:** Clinicopathological characteristics of Nottingham Tenovus series

|  |  |  |
| --- | --- | --- |
| **Variable** | **n\*** | **Cases (%)** |
| **Menopausal status** | 1650 |  |
| Pre-menopausal |  | 612 (37.0) |
| postmenopausal |  | 1038 (63.0) |
| **Tumour Grade (NGS)** | 1650 |  |
| G1 |  | 306 (18.5) |
| G2 |  | 531 (32.2) |
| G3 |  | 813 (49.3) |
| **Lymph node stage** | 1650 |  |
| Negative |  | 1056 (64.0) |
| Positive (1-3 nodes) |  | 486 (29.5) |
| Positive (>3 nodes) |  | 108 (6.5) |
| **Tumour size (cm)** | 1650 |  |
| T1 a + b (≤1.0) |  | 187 (11.0) |
| T1 c (>1.0 -2.0) |  | 868 (53.0) |
| T2 (>2.0-5) |  | 579 (35.0) |
| T3 (>5) |  | 16 (1.0) |
| **Tumour type** | 1650 |  |
| IDC-NST |  | 941 (57) |
| Tubular |  | 349 (21) |
| ILC |  | 160 (10) |
| Medullary (typical/atypical) |  | 41 (2.5) |
| Others |  | 159 (9.5) |
| **NPI subgroups** | 1650 |  |
| Excellent PG(2.08-2.40) | Low risk | 207 (12.5) |
| Good PG(2.42-3.40) | 331 (20.1) |
| Moderate I PG(3.42 to 4.4) | High risk | 488 (29.6) |
| Moderate II PG(4.42 to 5.4) | 395 (23.9) |
| Poor PG(5.42 to 6.4) | 170 (10.3) |
| Very poor PG(6.5–6.8) | 59 (3.6) |
| **Survival at 20 years** | 1650 |  |
| Alive and well |  | 1055 (64.0) |
| Dead from disease |  | 468 (28.4) |
| Dead from other causes |  | 127 (7.6) |
| **Adjuvant systemic therapy (AT**) |  |  |
| No AT |  | 665 (42.0) |
| Hormone therapy (HT) |  | 642 (41.0) |
| Chemotherapy (CMF) |  | 307 (20.0) |
| Hormone + chemotherapy |  | 46 (3.0) |

\* Number of cases for which data were available.

NPI; Nottingham prognostic index, PG; prognostic group

**Supplemental Table S2:** Clinicopathological characteristics of ER- cohort

|  |  |  |
| --- | --- | --- |
| **Variable** |  | **Cases (%)** |
| **Menopausal status** | 279 |  |
| Pre-menopausal |  | 119 (43.6) |
| postmenopausal |  | 154 (56.4) |
| **Tumour Grade (NGS)** | 279 |  |
| G1 |  | 1 (0.4) |
| G2 |  | 26 (9.5) |
| G3 |  | 248 (90.2) |
| **Tumour size (cm)** | 279 |  |
| ≤2.0 |  | 140 (52.6) |
| >2.0 |  | 126 (47.4) |
| **Mitotic index** | 279 |  |
| M1 |  | 21 (7.5) |
| M2 |  | 47(16.8) |
| M3 |  | 274 (98.9) |
| **Tubule formation** | 279 |  |
| 1 |  | 1 (0.4) |
| 2 |  | 36 (15.0) |
| 3 |  | 240 (86.6) |
| **Pleomorphism** | 279 |  |
| 1 |  | 0 (0) |
| 2 |  | 3 (1.1) |
| 3 |  | 274(98.9) |
| **Her-2 status** | 279 |  |
| Positive |  | 28 (10) |
| Negative |  | 251 (90) |
| **NPI** | 279 |  |
| Good (≤ 3.4) |  | 15 (5.5) |
| Moderate (3.41-5.4) |  | 194 (71.1) |
| Poor (>5.4) |  | 64 (23.4) |

NPI; Nottingham prognostic index, PG; prognostic group

**Supplementary Table S3:** Antigens, primary antibodies, clone, source, optimal dilution and scoring system used for each immunohistochemical marker

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Antigen** | **Antibody** | **Clone** | **Source** | **Antigen Retrieval** | **Dilution / Incubation Time** | **Distribution** | **Scoring**  **system** | **Cut-offs** |
| BRCA1 | BRCA1 | MS110 | Calbiochem | Citrate pH6 | 1:100  60 min | Nuclear | % of positive cells | <25% (negative) |
| ATM | Rabbit MAb anti-ATM | Y170 | Abcam | Citrate pH6 | 1:100  18 hours | Nuclear | % of positive cells | <25% (negative) |
| XRCC1 | Mouse MAb Anti-XRCC1 | 33-2-5 | Thermo-scientific | Citrate pH6 | 1:200  20 min | Nuclear | % of positive cells | ≥10% (positive) |
| Pol β | Rabbit anti-polβ | Ab26343 | Abcam | Citrate pH6 | 1:200  60 min | Nuclear | H- Score | ≥100  (Median H-score, positive) |
| BLM | Rabbit anti BLM | Polyclonal | Novus-Biologicals | Citrate pH6 | 1:100  18 Hours | Nuclear | H- Score | ≥50  (Median H-score, positive) |
| WRN | Rabbit Anti-WRN | Polyclonal | Novus  Biologicals | Citrate pH6 | 1:100  Overnight (18h) | Nuclear | H-score | Nuclear ≥116(Median H-score High) |
| RECQL4 | Rabbit Anti  RECQL4 | Polyclonal | Novus Biologicals | Citrate pH6 | 1:1000  60 min | Nuclear | H-score | Nuclear ≥215 (Median H-score High) |
| Ku70/  Ku80 | Mouse Anti-Ku70/Ku80 | Monoclonal | Abcam | Citrate pH6 | 1:2500  60 min | Nuclear | H- Score | >90  (X-tile cut-off, positive) |
| CHK2 | Rabbit Anti  CHK2 | Polyclonal | Abcam | Citrate pH6 | 1:100  60 min | Nuclear | H- Score | ≥100  (Median H-score, positive) |
| PARP1 | Mouse MAb Anti-PARP1 | 7D3-6 | BD pharmingen | Citrate pH6 | 1:1000 | Nuclear | % of positive cells | ≥10% (positive) |
| TOP2A | Mouse MAb | KiS1 | Dako-Cytomation | Citrate pH6 | 1:150  60 min | Nuclear | % of positive cells | >25% (positive) |
| FEN1 | Rabbit anti-FEN1 | polyclonal | Novus Biologicals | Citrate pH6 | 1:200  60 min | Nuclear | H-score | >100 (positive) |
| DNA-PKcs | Mouse MAb Anti- | 3H6 | Abcam | Citrate pH6 | 1:1000  20 min | Nuclear | H-score | >260 ((Mean H-score, positive) |
| ER | Mouse MAb anti-ER-α | SP1 | Dako-Cytomation | Citrate pH6 | 1:150  30 min | Nuclear | Allred score | ≥3 (positive) |
| ER | Mouse MAb anti-ER-α | EP1 | Dako-Cytomation | Citrate pH6 | 1:80  30 min | Nuclear | % positive cells | ≥1% positive |
| PR | Mouse MAb anti-PR | PgR636 | Dako-Cytomation | Citrate pH6 | 1:125  30 min | Nuclear | % positive cells | ≥1% positive |
| HER2 | Rabbit antihuman c-erbB2 | polyclonal | Dako-Cytomation | None | 1:400  60 min | Membrane | See text | See text |
| CD8 | Mouse MAb Anti-CD8 | 1A5 | Vector Laboratories | Citrate pH6 | 1:50  20 min | Membrane | See text | See text |
| FOXP3 | Mouse MAb Anti-FOXP3 | 236A/E7 | Abcam | Citrate pH6 | 1:100  60 min | Stroma | positive cell counts | ≥3 positive |
| PD-1 | Mouse MAb Anti-PD-1 | EH33 | Cell Signalling Technology | Citrate pH6 | 1:75  24 hours | Stroma | % positive cells | ≥5% positive |
| PD-L1 | Rabbit MAb Anti-PD-L1 | E1L3N | Cell Signalling Technology | Epitope retrieval solution 2, pH9, 95°C, 45 min | 1:25  24 hours | Membrane  Cytoplasm  Stroma | % positive in tumour  % positive cells in stroma | ≥1% positive |

All sections were pre-treated with microwave antigen retrieval using 0.1% citrate buffer (pH 6) except for HER2 (no pre-treatment).

**Supplementary Table S4:** Clinicopathological significance of ATM expression in CD8+ TILs positive and CD8+ TILs negative breast cancer

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **CD8 and ATM expression** | | | | **P- value** | **\*P -Value**  (Adjusted) |
| ATM+  /CD8+ | ATM+  /CD8- | ATM-  /CD8+ | ATM-  /CD8- |
| **A) Pathological Parameters** | | | | | | |
| **Tumour Size**  <1cm  >1-2cm  >2-5cm  >5cm | 30 (34.9%)  165(38.3%)  91(32.6%)  3 (21.4%) | 5 (5.8%)  51(11.8%)  27(9.7%)  2(14.3%) | 41 (47.7%)  176(40.8)  141(50.5)  8 (57.1%) | 10 (11.6)  39(9.0%)  20 (1.2%)  1 (7.1%) | 0.268 | 0.2924 |
| **Tumour Stage**  1  2  3 | 191(37.3%)  77 (32.8%)  21(33.3%) | 59(11.5%)  25(10.6%)  2 (3.2%) | 214(41.8%)  114(48.5%)  38 (60.3%) | 48 (9.4%)  19(8.1%)  2 (3.2%) | 0.054 | 0.0810 |
| **Tumour Grade**  G1  G2  G3 | 57 (46.0%)  100(38.3%)  132(31.0%) | 20(16.1%)  26(10.0%)  40(9.4%) | 40 (32.3)  110(42.1)  216(50.7) | 7 (5.6%)  25(9.6%)  38(8.9%) | 0.002 | **0.0080** |
| **NPI**  ≤ 3.4  >3.4 | 100(41.7%)  178(33.1%) | 30(12.5%)  53(9.9%) | 90(37.5%)  258(48.0%) | 20(8.3%)  49(9.1%) | 0.034 | 0.0680 |
| **Mitotic Index**  M1 (low; mitoses < 10)  M2 (medium; mitoses 10-18)  M3 (high; mitosis >18) | 116(43.8%)  54 (36.5%)  116(30.2%) | 28(10.6%)  16(10.8%)  37(9.6%) | 104(39.2%)  62 (41.9%)  195(50.8%) | 17(6.4%)  16(10.8%)  36(9.4%) | 0.014 | **0.0336** |
| **Tubule Formation**  1 (>75% definite tubule)  2 (10%-75% definite tubule)  3 (<10% definite tubule) | 12(27.3%)  111(43.5%)  163(32.7%) | 8(18.2%)  31(12.2%)  42(8.4%) | 19(43.2%)  88(34.5%)  254(51.0%) | 5(11.4%)  25(9.8%)  39(7.8%) | 0.001 | **0.0120** |
| **Pleomorphism**  1 (small-regular uniform)  2 (Moderate variation)  3 (Marked variation) | 6 (35.3%)  112(38.2%)  167(34.5%) | 3 (17.6%)  39(13.3%)  38(7.9%) | 6 (35.3%)  116(39.6%)  238(49.2%) | 2(11.8%)  26(8.9%)  41(8.5%) | 0.077 | 0.1027 |
| **Tumour Type**  IDC-NST  Tubular  Medullary  ILC  Others  Mixed NST &lobular/ special type | 165 (33.8%)  70 (42.9%)  10 (34.5%)  23 (33.8%)  2 (22.2%)  16 (37.2%) | 48 (9.8%)  24 (14.7%)  1 (3.4%)  4 (5.9%)  1 (11.1%)  6 (14.0%) | 236 (48.4%)  56 (34.4%)  17 (58.6%)  35 (51.5%)  5 (55.6%)  13 (30.2%) | 39 (8.0%)  13 (8.0)  1 (3.4%)  6 (8.8%)  1 (11.1%)  8 (18.6%) | 0.045 | 0.0836 |
| **HER-2 overexpression**  No  Yes | 243(35.8%)  41 (34.2%) | 76 (11.2%)  9 (7.5%) | 300(44.2%)  61 (50.8%) | 60(8.8%)  9 (7.5%) | 0.459 | 0.9670 |
| **ER**  Negative  Positive | 6.6 (29.6%)  220 (38.0%) | 15 (6.7%)  71 (12.3%) | 121(54.3%)  242(41.8%) | 21(9.4%)  46(7.9%) | 0.003 | **0.0098** |
| **PR**  Negative  Positive | 104(31.4%)  175(38.5%) | 23(6.9%)  62(13.6%) | 172(52.0%)  180(39.6%) | 32(9.7%)  38(8.4%) | 0.001 | **0.0130** |

**Supplementary Table S5:** Clinicopathological significance of BRCA1 expression in CD8 positive and CD8 negative breast cancer

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | | | | **P- value** | **\*P -Value**  (Adjusted) |
| BRCA1+  /CD8+ | BRCA1+  /CD8- | BRCA1-  /CD8+ | BRCA1-  /CD8- |
| **A) Pathological Parameters** | | | | | | |
| **Tumour Size**  <1cm  >1-2cm  >2-5cm  >5cm | 79 (77.5%)  363(68.6%)  278(68.3%)  10 (50%) | 15 (14.7%)  86(16.3%)  51 (12.5%)  3 (15%) | 6 (5.9%)  64 (12.1%)  70(17.2%)  6 (30%) | 2 (2.0%)  16(3.0%)  8 (2.0%)  1 (5.0%) | 0.26 | 0.624 |
| **Tumour Stage**  1  2  3 | 418(65.3%)  245(74.7%)  67 (73.6%) | 107(16.7%)  41 (12.5%)  8 (8.8%) | 95(14.8%)  36(11.0%)  15(16.5%) | 20(3.1%)  6 (1.85%)  1 (1.1%) | 0.40 | 0.8 |
| **Tumour Grade**  G1  G2  G3 | 112(68.7%)  263(78.0%)  355(63.5%) | 33 (20.2%)  53 (15.7%)  70 (12.5%) | 10 (6.1%)  18 (5.3%)  118(21.1%) | 8 (4.9%)  3 (0.9%)  16(2.9%) | 3.5x10-12 | **p<0.0001** |
| **NPI**  ≤ 3.4  >3.4 | 218(72.7%)  474(66.9%) | 58 (18.7%)  94 (13.3%) | 18 (6.0%)  121 (17.1%) | 8 (2.7%)  19 (2.7%) | 0.000026 | **0.0003** |
| **Mitotic Index**  M1 (low; mitoses < 10)  M2 (medium; mitoses 10-18)  M3 (high; mitosis >18) | 260 (76.9%)  142 (73.2%)  317 (63.4%) | 56 (16.6%)  29 (14.9%)  62 (12.4%) | 17 (5.0%)  19 (9.8%)  106(21.2%) | 5 (1.5%)  4 (2.1%)  15(3.0%) | 2.4x10-9 | **p<0.0001** |
| **Tubule Formation**  1 (>75% definite tubule)  2 (10%-75% definite tubule)  3 (<10% definite tubule) | 36 (64.3%)  231(70.6%)  452(69.2%) | 14(25.0%)  56(17.1%)  77(11.9%) | 2 (3.6%)  33 (10.1%)  107(16.5%) | 56 (100%)  327(100%)  649(100%) | 0.000207 | **0.0012** |
| **Pleomorphism**  1 (small-regular uniform)  2 (Moderate variation)  3 (Marked variation) | 13 (86.7%)  282(73.2%)  421(67.0%) | 0 (0%)  74(19.2%)  72(11.5%) | 0 (0%)  22 (5.7%)  120(19.1%) | 2 (13.3%)  7 (1.8%)  15 (2.4%) | 3.5x10-10 | **p<0.0001** |
| **Tumour Type**  IDC-NST  Tubular  Medullary  ILC  Others  Mixed NST& Lobular special type | 418 (66.5%)  144(70.6%)  18 (56.3%)  96 (85.7%)  9 (75%)  38 (65.5%) | 82 (13%)  40 (19.6%)  1 (3.1%)  13 (11.6%)  3 (25%)  16 (27.6%) | 113 (18%)  11 (5.4%)  12 (37.5%)  3 (2.7%)  0 (0%)  3 (5.2%) | 16 (2.5%)  9 (4.4%)  1 (3.1%)  0 (0 %)  1 (1.7%)  27 (2.6%) | 6.4x10-10 | **p <0.0001** |
| **HER-2**  Negative  Positive | 626(69.0)  95 (66.4) | 140 (15.4)  16 (11.2) | 116 (12.8)  30 (21.0) | 25 (2.8)  2 (1.4) | 0.037 | 0.1418 |
| **ER**  Negative  Positive | 150 (55.8%)  574 (74.1%) | 28 (10.4%)  124 (16.0%) | 76 (28.3%)  66 (8.5%) | 15 (5.6%)  11 (1.4%) | 2.6x10-18 | **p<0.0001** |
| **PR**  Negative  Positive | 260 (61.2%)  464 (74.1%) | 47 (11.1%)  108(17.3%) | 101 (23.8%)  44 (7.0%) | 17 (4.0%)  10 (1.6%) | 4.6x10-15 | **p<0.0001** |

**Supplementary Table S6**: Clinicopathological significance of XRCC1 expression in CD8 positive and CD8 negative breast cancers

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **CD8 and XRCC1 expression** | | | | | | **P- value** | | **\*P -Value**  (Adjusted) | |
| XRCC1+  /CD8+ | XRCC1+  /CD8- | XRCC1-  /CD8+ | | XRCC1-  /CD8- | |
| **A) Pathological Parameters** | | | | | | | | | | |
| **Tumour Size**  <1cm  >1-2cm  >2-5cm  >5cm | 61 (71.8%)  346 (76.8%)  254(67.6%)  12 (63.2%) | 11(12.9%)  90(17.6%)  52(13.8%)  3 (15.8%) | | 11(12.9%)  52(10.2%)  62(16.5%)  3 (15.8%) | | 2 (2.4%)  22(4.3%)  8 (2.1%)  1 (5.3%) | | 0.161 | | 0.1756 |
| **Tumour Stage**  1  2  3 | 393(66.3%)  209(67.9%)  71 (78.0%) | 106(17.9%)  45 (14.6%)  7 (7.7%) | | 67(11.3%)  49(15.9%)  11(12.1%) | | 27(4.6%)  5 (1.6%)  2 (2.2%) | | 0.013 | | **0.0173** |
| **Tumour Grade**  G1  G2  G3 | 97 (66%)  238(75.8%)  71 (78%) | 33(22.4%)  51 (16.2%)  73 (13.8%) | | 12(8.2%)  17(5.4%)  99(18.7%) | | 5 (3.4%)  8 (2.5%)  20(3.8%) | | 3.5x10-7 | | **p<0.0001** |
| **NPI**  ≤ 3.4  >3.4 | 196(71.3%)  442(65.7%) | 54(19.6%)  99(14.7%) | | 16(5.8%)  108(16%) | | 9 (3.3%)  24(3.6%) | | 0.000214 | | **0.0004** |
| **Mitotic Index**  M1 (low; mitoses < 10)  M2 (medium; mitoses 10-18)  M3 (high; mitosis >18) | 231(74.3%)  128(70.3%)  301 (64%) | 53 (17%)  28(15.4%)  64(13.6%) | | 20 (6.4%)  18 (9.9%)  89 (18.9%) | | 7(2.3%)  8(4.4%)  16(3.4%) | | 0.000036 | | **0.0001** |
| **Tubule Formation**  1 (>75% definite tubule)  2 (10%-75% definite tubule)  3 (<10% definite tubule) | 26(56.5%)  211(68.7%)  423(69.3%) | 16 (34.8%)  53(17.3%)  76 (12.5%) | | 3 (6.5%)  31(10.1%)  93 (15.2%) | | 1(2.2%)  12(3.9%)  18(3.0%) | | 0.001 | | **0.0015** |
| **Pleomorphism**  1 (small-regular uniform)  2 (Moderate variation)  3 (Marked variation) | 14 (87.5%)  254(71.1%)  389(66.5%) | 2 (12.5%)  70 (19.6%)  143(14.9%) | | 0 (0)  23(6.4%)  104(17.8) | | 0 (0)  10(2.8%)  21(3.6%) | | 0.000005 | | **p <0.0001** |
| **Tumour Type**  IDC-NST  Tubular  Medullary  ILC  Others  Mixed NST & Lobular/special type | 408(67.4%)  120(64.5%)  18(64.3%)  81(82.7%)  6 (54.5%)  31(62%) | 86(14.2%)  42(22.6%)  0 (0)  10(10.2%)  3 (27.3%)  12(24%) | | 93(15.4%)  17(9.1%)  8 (28.6%)  5 (5.1%)  1 (9.1%)  4 (8%) | | 18(3.0%)  7 (3.8%)  2 (7.1%)  2 (2.0%)  1 (9.1%)  3 (6%) | | 0.000485 | | **0.0008** |
| **Her2 overexpression**  No  Yes | 571(67.6%)  92 (67.2%) | 139(16.4%)  19 (13.9%) | | 107(12.7)  22 (16.1%) | | 28(3.3%)  4 (2.9%) | | 0.663 | | 7.9560 |
| **ER**  Negative  Positive | 148(59.0%)  512(71.2%) | 29(11.6%)  124(17.2%) | | 60(23.9%)  66(9.2%) | | 14(5.6%)  17(2.4%) | | 9.3x10-7 | | **p <0.0001** |
| **PR**  Negative  Positive | 240(60.8%)  401(71.7%) | 56(14.2%)  100(17.9%) | | 80(20.3%)  45(8.1%) | | 19(4.8%)  13(2.3%) | | 5.4x10-8 | | **p <0.0001** |

**Supplementary Table S7:** Clinicopathological significance of ATM expression in FOXP3 positive and FOXP3negative breast cancer

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **FOXP3 and ATM expression** | | | | **P- value** | **\*P -Value**  (Adjusted) |
| ATM+  / FOXP3+ | ATM+  / FOXP3- | ATM-  / FOXP3+ | ATM-  / FOXP3- |
| **A) Pathological Parameters** | | | | | | |
| **Tumour Size**  <1cm  >1-2cm  >2-5cm  >5cm | 19 (20%)  145 (30.7%)  81 (27.7%)  2 (15.4%) | 25 (26.3%)  103 (21.8%)  41 (14%)  2 (15.4%) | 31 (32.6  154( 32.6  113 (38.7  6 (46.2 | 20 (21.1  71 (15  57(19.5  3 (23.1 | 0.036 | 0.3960 |
| **Tumour Stage**  1  2  3 | 157 (28.4%)  71 (28.2%)  19 (27.9%) | 122 (22.1%)  42 (16.7%)  8 (11.8%) | 185 (33.5%)  87 (34.5%)  32 (47.1%) | 89 (16.1%)  52 (20.6%)  9 (13.2%) | 0.092 | 0.5060 |
| **Tumour Grade**  G1  G2  G3 | 40 (28%)  66 (23.1%)  141(31.7%) | 56 (39.2%)  73 (25.5%)  43 (9.7%) | 26 (18.2%)  74 (25.9%)  204 (45.8%) | 21 (14.7%)  73 (25.5%)  57 (12.8%) | 1.7X 10-21 | **<0.0001** |
| **NPI**  ≤ 3.4  >3.4 | 69 (25.9%)  170(29.6%) | 84 (31.6%)  82 (14.3%) | 64 (24.1%)  226 (39.3%) | 49 (18.4%)  97 (16.9%) | 6.5 X10-9 | **<0.0001** |
| **Mitotic Index**  M1 (low; mitoses < 10)  M2 (medium; mitoses 10-18)  M3 (high; mitosis >18) | 72 (24.2%)  44 (27.2%)  126 (31.4%) | 99 (33.3%)  32 (19.8%)  39 (9.7%) | 66 (22.2%)  53 (32.7%)  183(45.6%) | 60 (20.2%)  33 (20.4%)  53 (13.2%) | 4.1x10-16 | **<0.0001** |
| **Tubule Formation**  1 (>75% definite tubule)  2 (10%-75% definite tubule)  3 (<10% definite tubule) | 10 (20.4%)  82 (29.3%)  150 (28.2%) | 16 (32.7%)  80 (28.6%)  74 (13.9%) | 14 (28.6%)  70 (25%)  218(41.1%) | 9 (18.4%)  48(17.1%)  89(16.8%) | 5.5x10-7 | **<0.0001** |
| **Pleomorphism**  1 (small-regular uniform)  2 (Moderate variation)  3 (Marked variation) | 6 (30%)  83 (25.2%)  151(29.7%) | 7 (35%)  97(29.5%)  66 (13%) | 6 (30%)  74 (22.5%)  222 (43.7%) | 1 (5%)  75 (22.8%)  69 (13.6%) | 7.8x10-3 | **<0.0001** |
| **Tumour Type**  IDC-NST  Tubular  Medullary  ILC  Others  Mixed NST &lobular/ special type | 158 (30.6%)  51 (28%)  11 (36.7%)  10 (13%)  1 (12.5%)  12 (24.5%) | 72 (13.9%)  59 (32.4%)  1 (3.3%)  24 (31.4%)  2 (25%)  14 (28.6%) | 212 (41%)  41 (22.5%)  18 (60%)  17 (22.1%)  2 (25%)  11 (22.4%) | 75(14.5%)  31(17%)  0 (0%)  26(33.8%)  3 (37.5%)  12 (24.5%) | 4.4x10-13 | **<0.0001** |
| **HER-2 overexpression**  No  Yes | 198 (26.8%)  48 (39.8%) | 165(22.2%)  4 (3.3%) | 244 (32.9%)  57 (46.7%) | 135(18.2%)  13 (10.7%) | 1.6x10-7 | **<0.0001** |
| **ER**  Negative  Positive | 76 (32.2%)  168(26.8%) | 18 (7.6%)  153(24.4%) | 117 (49.6%)  181 (28.9%) | 25 (10.6%)  124(19.8%) | 4.7x10-12 | **<0.0001** |
| **PR**  Negative  Positive | 99 (28.7%)  140(27.9%) | 41 (11.9%)  123(24.6%) | 156 (45.2%)  141 (28.1%) | 49 (14.2%)  97 (19.4%) | 4.4x10-8 | **<0.0001** |

**Supplementary Table S8:** Clinicopathological significance of BRCA1 expression in FOXP3 positive and FOXP3negative breast cancer

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **FOXP3 and ATM expression** | | | | **P- value** | **\*P -Value**  (Adjusted) |
| BRCA1+  / FOXP3+ | BRCA1+  / FOXP3- | BRCA1-  / FOXP3+ | BRCA1-  / FOXP3- |
| **A) Pathological Parameters** | | | | | | |
| **Tumour Size**  <1cm  >1-2cm  >2-5cm  >5cm | 60 (51.3%)  308(54.4%)  230(54.1%)  8 (38.1%) | 48 (41%)  177(31.3%)  118 (27.8%)  6 (28.6%) | 5 (4.3%)  58(10.2%)  60(14.1%)  6 (28.6%) | 4 (3.4%)  23(4.1%)  17(4%)  1 (4.8%) | 0.015 | **0.0165** |
| **Tumour Stage**  1  2  3 | 354 (51.5%)  196 (56.5%)  56 (58.3%) | 217 (31.6%)  109 (109%)  24 (25%) | 86 (12.5%)  31 (8.9%)  12 (12.5%) | 30 (4.4%)  11 (3.2%)  4 (4.2%) | 0.397 | 4.3670 |
| **Tumour Grade**  G1  G2  G3 | 81 (44.3%)  176 (47.4%)  349 (60.6%) | 83 (45.4%)  170(45.8%)  97 (16.8%) | 5 (2.7%)  15 (4%)  109 (18.9%) | 14 (7.7%)  10 (2.7%)  21 (3.6%) | 2.0X10-30 | **<0.0001** |
| **NPI**  ≤ 3.4  >3.4 | 161 (48.3%)  416 (55.7%) | 143 (42.9%)  192 (25.7%) | 13 (3.9%)  112 (15%) | 16 (4.8%)  27 (3.6%) | 9.3 X10-11 | **<0.0001** |
| **Mitotic Index**  M1 (low; mitoses < 10)  M2 (medium; mitoses 10-18)  M3 (high; mitosis >18) | 171 (45.1%)  108 (51.9%)  312 (60.7%) | 183(48.3%)  76 (36.5%)  84 (16.3%) | 11 (2.9%)  17 (8.2%)  97 (18.9%) | 14 (3.7%)  7 (3.4%)  21 (4.1%) | 9.5X10-27 | **<0.0001** |
| **Tubule Formation**  1 (>75% definite tubule)  2 (10%-75% definite tubule)  3 (<10% definite tubule) | 26 (44.1%)  178(49.7%)  387(56.6%) | 26 (44.1%)  139(38.8%)  178(26%) | 0 (0%)  25 (7%)  100(14.6%) | 7 (11.9%)  16(4.5%)  19(2.8%) | 4.0x10-9 | **<0.0001** |
| **Pleomorphism**  1 (small-regular uniform)  2 (Moderate variation)  3 (Marked variation) | 8 (42.1%)  204(47.8%)  376(57.8%) | 9 (47.4%)  191(44.7%)  142(21.8%) | 1 (5.3%)  12 (2.8%)  112(17.2%) | 1 (5.3%)  20(4.7%)  21(3.2%) | 3.3x10-19 | **<0.0001** |
| **Tumour Type**  IDC-NST  Tubular  Medullary  ILC  Others  Mixed NST &lobular/ special type | 383(58.4%)  107(47.6%)  19 (59.4%)  56 (44.4%)  6 (54.5%)  29 (43.3%) | 145 (22.1%0  96 (42.7%)  0 (0%)  68 (54%)  5 (45.5%)  33 (49.3%) | 102 (15.5%)  9 (4%)  13 (40.6%)  1 (0.8%)  0 (0%)  1 (1.5%) | 26 (4%)  13 (5.8%)  0 (0%)  1 (0.8%)  0 (0%)  4 (6%) | 1.5x10-23 | **<0.0001** |
| **HER-2 overexpression**  No  Yes | 511(52.3%)  93 (64.1%) | 323(33.1%)  21 (14.5%) | 101(10.3%)  28 (19.3%) | 42 (4.3%)  3 (2.1%) | 0.000004 | **<0.0001** |
| **ER**  Negative  Positive | 163 (58%)  431 (52%) | 29 (10.3%)  318(38.4%) | 72 (25.6%)  53 (6.4%) | 17 (6%)  27 (3.3%) | 2.1x10-27 | **<0.0001** |
| **PR**  Negative  Positive | 239 (54.7%)  363 (53.5%) | 85 (19.5%)  256(37.8%) | 90 (20.6%)  37 (5.5%) | 23 (5.3%)  22 (3.2%) | 2.2x10-18 | **<0.0001** |

**Supplementary Table S9:** Clinicopathological significance of XRCC1 expression in FOXP3 positive and FOXP3negative breast cancer.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **FOXP3 and ATM expression** | | | | **P- value** | **\*P -Value**  (Adjusted) |
| XRCC1+  / FOXP3+ | XRCC1+  / FOXP3- | XRCC1-  / FOXP3+ | XRCC1-  / FOXP3- |
| **A) Pathological Parameters** | | | | | | |
| **Tumour Size**  <1cm  >1-2cm  >2-5cm  >5cm | 45 (45.5%)  293(53.5%)  206(52.3%)  10 (52.6%) | 39 (39.4%)  176(32.1%)  111(28.2%)  5 (26.3%) | 9 (9.1%)  52 (9.5%)  55 (14%)  4 (21.1%) | 6 (6.1%)  28(5.1%)  22 (5.6%)  0 (0%) | 0.219 | 2.4090 |
| **Tumour Stage**  1  2  3 | 340 (52.5%)  158 (49.1%)  57 (60.6%) | 204 (31.5%)  107 (33.2%)  22 (23.4%) | 63 (9.7%)  43 (13.4%)  14 (14.9%) | 41 (6.3%)  14 (4.3%)  1 (1.1%) | 0.044 | 0.0484 |
| **Tumour Grade**  G1  G2  G3 | 74 (41.8%)  157(45.8%)  323 (59.6%) | 81 (45.8%)  158(46.1%)  93 (17.2%) | 8 (4.5%)  9 (2.6%)  103 (19%) | 14 (7.9%)  19 (5.5%)  23 (4.2%) | 1.1 X10-28 | **<0.0001** |
| **NPI**  ≤ 3.4  >3.4 | 150 (47.8%)  379 (53.7%) | 134 (42.7%)  187 (26.5%) | 10 (3.2%)  104(14.7%) | 20 (6.4%)  36 (5.1%) | 5.3X10-10 | **<0.0001** |
| **Mitotic Index**  M1 (low; mitoses < 10)  M2 (medium; mitoses 10-18)  M3 (high; mitosis >18) | 154 (43.1%)  101(52.3%)  282(58.8%) | 170(47.6%)  63 (32.6%)  87 (18.1%) | 14 (3.9%)  14 (7.3%)  92 (19.2%) | 19 (5.3%)  15 (7.8%)  19 (4%) | 1.2x10-22 | **0.0001** |
| **Tubule Formation**  1 (>75% definite tubule)  2 (10%-75% definite tubule)  3 (<10% definite tubule) | 22 (43.1%)  168(48.3%)  347(55%) | 22 (43.1%)  136(39.1%)  162(25.7%) | 2 (3.9%)  19(5.5%)  99(15.7%) | 5 (9.8%)  25(7.2%)  23(3.6%) | 7.8x10-9 | **<0.0001** |
| **Pleomorphism**  1 (small-regular uniform)  2 (Moderate variation)  3 (Marked variation) | 10 (41.7%)  177(44.5%)  346(57.4%) | 11 (45.8%)  183(46%)  125(20.7%) | 1 (4.2%)  15(3.8%)  104(17.2%) | 2 (8.3%)  23(5.8%)  28(4.6%) | 5.2x10-19 | **<0.0001** |
| **Tumour Type**  IDC-NST  Tubular  Medullary  ILC  Others  Mixed NST &lobular/ special type | 370 (59.2%)  92 (43.2%)  17 (60.7%)  38 (34.2%)  3 (23.1%)  26 (42.6%) | 137 (21.9%)  92 (43.2%)  1 (3.6%)  64 (57.7%)  8 (61.5%)  26 (42.6%) | 92 (14.7%)  11 (5.2%)  10 (35.7%)  4 (3.6%)  0 (0%)  3 (4.9%) | 26 (4.2%)  17 (8%)  0 (0%)  5 (4.5%)  2 (15.4%)  6 (9.8%) | 5.1x10-21 | **<0.0001** |
| **HER-2 overexpression**  No  Yes | 458 (50.2%)  93 (66.9%) | 308 (33.7%)  18 (12.9%) | 100 (11%)  21 (15.1%) | 47 (5.1%)  7 (5%) | 0.000015 | **<0.0001** |
| **ER**  Negative  Positive | 151 (58.8%)  390 (50.1%) | 27 (10.5%)  298 (38.3%) | 61 (23.7%)  55 (7.1%) | 18 (7%)  35 (4.5%) | 1.19x10-21 | **<0.0001** |
| **PR**  Negative  Positive | 216 (53.5%)  316 (52%) | 83 (20.5%)  229(37.7%) | 80 (19.8%)  35 (5.8%) | 25 (6.2%)  28 (4.6%) | 2.4x10-14 | **<0.0001** |