SUPPLEMENTARY INFORMATION

Real-world clinical outcomes of patients with BRCA-mutated, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer: a CancerLinQ® study

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Table S1  Treatment received post mBC diagnosis by therapy class (stratified by BRCA status)

| First-line therapy class                | BRCAm ($n = 83$) | BRCAwt ($n = 460$) | BRCAu ($n = 3201$) | All patients ($N = 3744$) |
|-----------------------------------------|------------------|-------------------|-------------------|--------------------------|
| CDK4/6 inhibitor-based therapy          | 8 (11.1)         | 57 (13.5)         | 326 (11.6)        | 391 (11.8)               |
| Chemotherapy + endocrine therapy        | 4 (5.6)          | 17 (4.0)          | 104 (3.7)         | 125 (3.8)                |
| Chemotherapy only                       | 35 (48.6)        | 191 (45.3)        | 924 (32.9)        | 1150 (34.8)              |
| Endocrine therapy only                  | 21 (29.2)        | 125 (29.6)        | 1259 (44.8)       | 1405 (42.5)              |
| HER2-targeted-based therapy             | 0 (0.0)          | 9 (2.1)           | 26 (0.9)          | 35 (1.1)                 |
| mTOR inhibitor-based therapy            | 1 (1.4)          | 4 (0.9)           | 55 (2.0)          | 60 (1.8)                 |
| Other therapy                           | 3 (4.2)          | 16 (3.8)          | 111 (3.9)         | 130 (3.9)                |
| PARP inhibitor-based therapy            | 0 (0.0)          | 0 (0.0)           | 1 (0.0)           | 1 (0.0)                  |
| PD-1/PD-L1-based therapy               | 0 (0.0)          | 3 (0.7)           | 5 (0.2)           | 8 (0.2)                  |
| Missing                                 | 11               | 38                | 390               | 439                      |

| Second-line therapy class               |                  |                   |                   |                          |
|-----------------------------------------|------------------|-------------------|-------------------|--------------------------|
| CDK4/6 inhibitor-based therapy          | 9 (16.1)         | 46 (15.5)         | 323 (17.3)        | 378 (17.0)               |
| Chemotherapy + endocrine therapy        | 2 (3.6)          | 17 (5.7)          | 148 (7.9)         | 167 (7.5)                |
| Chemotherapy only                       | 24 (42.9)        | 118 (39.9)        | 596 (31.9)        | 738 (33.2)               |
| Therapy Class                              | Third-line | Fourth-line | Fifth-line | Sixth-line |
|-------------------------------------------|------------|-------------|------------|------------|
| Endocrine therapy only                    | 14 (25.0)  | 72 (24.3)   | 620 (33.2) | 706 (31.8) |
| HER2-targeted-based therapy               | 1 (1.8)    | 7 (2.4)     | 20 (1.1)   | 28 (1.3)   |
| mTOR inhibitor-based therapy              | 3 (5.4)    | 15 (5.1)    | 80 (4.3)   | 98 (4.4)   |
| Other therapy                             | 2 (3.6)    | 16 (5.4)    | 74 (4.0)   | 92 (4.1)   |
| PARP inhibitor-based therapy              | 1 (1.8)    | 1 (0.3)     | 2 (0.1)    | 4 (0.2)    |
| PD-1/PD-L1-based therapy                  | 0 (0.0)    | 4 (1.4)     | 7 (0.4)    | 11 (0.5)   |
| Missing                                   | 27         | 164         | 1331       | 1522       |

Third-line therapy class

| Therapy Class                              | Third-line | Fourth-line | Fifth-line | Sixth-line |
|-------------------------------------------|------------|-------------|------------|------------|
| CDK4/6 inhibitor-based therapy            | 11 (27.5)  | 31 (14.9)   | 200 (15.9) | 242 (16.0) |
| Chemotherapy + endocrine therapy          | 2 (5.0)    | 21 (10.1)   | 118 (9.4)  | 141 (9.4)  |
| Chemotherapy only                         | 12 (30.0)  | 74 (35.6)   | 449 (35.6) | 535 (35.5) |
| Endocrine therapy only                    | 10 (25.0)  | 55 (26.4)   | 363 (28.8) | 428 (28.4) |
| HER2-targeted-based therapy               | 0 (0.0)    | 5 (2.4)     | 15 (1.2)   | 20 (1.3)   |
| mTOR inhibitor-based therapy              | 3 (7.5)    | 13 (6.2)    | 68 (5.4)   | 84 (5.6)   |
| Other therapy                             | 0 (0.0)    | 4 (1.9)     | 39 (3.1)   | 43 (2.9)   |
| PARP inhibitor-based therapy              | 1 (2.5)    | 0 (0.0)     | 1 (0.1)    | 2 (0.1)    |
| PD-1/PD-L1-based therapy                  | 1 (2.5)    | 5 (2.4)     | 7 (0.6)    | 13 (0.9)   |
| Missing                                   | 43         | 252         | 1941       | 2236       |
Data are reported as number of patients (%). Percentage values have been calculated after excluding the $n$ for missing data from the denominator.

**BRCA BRCA1** and/or **BRCA2**; **BRCAm** BRCA-mutated; **BRCAu** unknown BRCA status; **BRCAwt** BRCA wild type; **CDK** cyclin-dependent kinase; **HER2** human epidermal growth factor receptor 2; **mBC** metastatic breast cancer; **mTOR** mechanistic target of rapamycin; **PARP** poly(ADP-ribose) polymerase; **PD-1** programmed cell death protein 1; **PD-L1** programmed death-ligand 1
| Table S2 | Treatment received post mBC diagnosis by therapy class (HR positive) |
|---------|-------------------------------------------------------------|
|         | BRCAm | BRCAwt | BRCAu | All patients |
|         | \((n = 47)\) | \((n = 296)\) | \((n = 2395)\) | \((n = 2738)\) |
| **First-line therapy class** | | | | |
| CDK4/6 inhibitor-based therapy | 8 (17.8) | 48 (17.3) | 308 (14.2) | 364 (14.6) |
| Chemotherapy + endocrine therapy | 3 (6.7) | 13 (4.7) | 89 (4.1) | 105 (4.2) |
| Chemotherapy | 15 (33.3) | 85 (30.7) | 485 (22.3) | 585 (23.4) |
| Endocrine therapy | 16 (35.6) | 115 (41.5) | 1161 (53.4) | 1292 (51.8) |
| HER-targeted based therapy | 0 (0.0) | 5 (1.8) | 17 (0.8) | 22 (0.9) |
| \(mTOR\) inhibitor-based therapy | 1 (2.2) | 4 (1.4) | 54 (2.5) | 59 (2.4) |
| Other therapy | 2 (4.4) | 6 (2.2) | 58 (2.7) | 66 (2.6) |
| PARP inhibitor-based therapy | 0 (0.0) | 0 (0.0) | 1 (0.0) | 1 (0.0) |
| PD-1/PD-L1 based therapy | 0 (0.0) | 1 (0.4) | 1 (0.0) | 2 (0.1) |
| Missing | 2 | 19 | 221 | 242 |
| **Second line therapy class** | | | | |
| CDK4/6 inhibitor-based therapy | 8 (22.2) | 39 (19.5) | 302 (20.3) | 349 (20.2) |
| Chemotherapy + endocrine therapy | 1 (2.8) | 16 (8.0) | 128 (8.6) | 145 (8.4) |
| Chemotherapy | 8 (22.2) | 48 (24.0) | 346 (23.2) | 402 (23.3) |
| Endocrine therapy | 13 (36.1) | 68 (34.0) | 571 (38.3) | 652 (37.8) |
| HER-targeted based therapy | 1 (2.8) | 6 (3.0) | 18 (1.2) | 25 (1.4) |
|                       | 3 (8.3) | 13 (6.5) | 74 (5.0) | 90 (5.2) |
|-----------------------|---------|----------|----------|----------|
| mTOR inhibitor-based therapy |         |          |          |          |
| Other therapy         | 1 (2.8) | 9 (4.5)  | 47 (3.2) | 57 (3.3) |
| PARP inhibitor-based therapy | 1 (2.8) | 0 (0.0)  | 2 (0.1)  | 3 (0.2)  |
| PD-1/PD-L1 based therapy | 0 (0.0) | 1 (0.5)  | 2 (0.1)  | 3 (0.2)  |
| Missing               | 11      | 96       | 905      | 1012     |

**Third line therapy class**

|                       | 10 (35.7) | 30 (20.4) | 183 (17.7) | 223 (18.4) |
|-----------------------|-----------|-----------|------------|------------|
| CDK4/6 inhibitor-based therapy |         |          |            |            |
| Chemotherapy + endocrine therapy | 2 (7.1)  | 16 (10.9) | 105 (10.2) | 123 (10.2) |
| Chemotherapy          | 6 (21.4)  | 32 (21.8) | 301 (29.1) | 339 (28.0) |
| Endocrine therapy     | 8 (28.6)  | 52 (35.4) | 335 (32.4) | 395 (32.7) |
| HER-targeted based therapy | 0 (0.0)  | 4 (2.7)   | 14 (1.4)   | 18 (1.5)   |
| mTOR inhibitor-based therapy | 2 (7.1)  | 10 (6.8)  | 62 (6.0)   | 74 (6.1)   |
| Other therapy         | 0 (0.0)   | 3 (2.0)   | 29 (2.8)   | 32 (2.6)   |
| PARP inhibitor-based therapy | 0 (0.0)  | 0 (0.0)   | 1 (0.1)    | 1 (0.1)    |
| PD-1/PD-L1 based therapy | 0 (0.0)  | 0 (0.0)   | 4 (0.4)    | 4 (0.3)    |
| Missing               | 19        | 149       | 1361       | 1529       |

Data are reported as number of patients (%). Percentage values have been calculated after excluding the n for missing values from the denominator.

BRCA1 and/or BRCA2; BRCA-mutated; BRCAu unknown BRCA status; BRCAwt BRCA wild type; CDK cyclin-dependent kinase; HER2 human epidermal growth factor receptor 2; HR hormone receptor; mBC metastatic breast cancer; mTOR mechanistic target of rapamycin; PARP
poly(ADP-ribose) polymerase; *PD-1* programmed cell death protein 1; *PD-L1* programmed death-ligand 1

**Table S3**  Treatment received post-mBC diagnosis by therapy class (TNBC)

|                               | BRCAm   | BRCAwt  | BRCAu   | All patients |
|-------------------------------|---------|---------|---------|--------------|
|                               | $(n = 29)$ | $(n = 130)$ | $(n = 609)$ | $(n = 768)$ |

**First-line therapy class**

| Treatment                   | BRCAm     | BRCAwt    | BRCAu     | All patients |
|-----------------------------|-----------|-----------|-----------|--------------|
| CDK4/6 inhibitor-based therapy | 0 (0.0) | 3 (2.7) | 2 (0.4) | 5 (0.8) |
| Chemotherapy + endocrine therapy | 1 (5.0) | 3 (2.7) | 6 (1.3) | 10 (1.7) |
| Chemotherapy                 | 17 (85.0) | 92 (81.4) | 382 (82.0) | 491 (82.0) |
| Endocrine therapy            | 1 (5.0) | 1 (0.9) | 26 (5.6) | 28 (4.7) |
| HER2-targeted-based therapy  | 0 (0.0) | 3 (2.7) | 6 (1.3) | 9 (1.5) |
| Other therapy                | 1 (5.0) | 9 (8.0) | 40 (8.6) | 50 (8.3) |
| PD-1/PD-L1-based therapy     | 0 (0.0) | 2 (1.8) | 4 (0.9) | 6 (1.0) |
| Missing                      | 9         | 17        | 143       | 169          |

**Second-line therapy class**

| Treatment                   | BRCAm     | BRCAwt    | BRCAu     | All patients |
|-----------------------------|-----------|-----------|-----------|--------------|
| CDK4/6 inhibitor-based therapy | 0 (0.0) | 0 (0.0) | 3 (1.1) | 3 (0.9) |
| Chemotherapy + endocrine therapy | 0 (0.0) | 0 (0.0) | 9 (3.4) | 9 (2.6) |
| Chemotherapy                 | 13 (92.9) | 57 (85.1) | 212 (80.3) | 282 (81.7) |
| Endocrine therapy            | 0 (0.0) | 0 (0.0) | 10 (3.8) | 10 (2.9) |
| Therapy Class                                      | HER2-targeted-based therapy | mTOR inhibitor-based therapy | Other therapy | PD-1/PD-L1-based therapy | Missing |
|---------------------------------------------------|-----------------------------|-------------------------------|---------------|--------------------------|---------|
| 0 (0.0) | 0 (0.0) | 1 (0.4) | 1 (0.3) | 0 (0.0) | 1 (1.5) | 2 (0.8) | 3 (0.9) | 1 (7.1) | 6 (9.0) | 23 (8.7) | 30 (8.7) | 0 (0.0) | 3 (4.5) | 4 (1.5) | 7 (2.0) | 15 | 63 | 345 | 423 |

| Third-line therapy class                           | CDK4/6 inhibitor-based therapy | Chemotherapy + endocrine therapy | Chemotherapy | Endocrine therapy | mTOR inhibitor-based therapy | Other therapy | PARP inhibitor-based therapy | PD-1/PD-L1-based therapy | Missing |
|---------------------------------------------------|-------------------------------|---------------------------------|--------------|------------------|-------------------------------|---------------|-----------------------------|--------------------------|---------|
| 0 (0.0) | 0 (0.0) | 3 (2.0) | 3 (1.5) | 0 (0.0) | 1 (2.4) | 4 (2.6) | 5 (2.5) | 5 (62.5) | 33 (80.5) | 114 (75.5) | 152 (76.0) | 0 (0.0) | 1 (2.4) | 3 (2.0) | 4 (2.0) | 1 (12.5) | 0 (0.0) | 15 (9.9) | 16 (8.0) | 1 (12.5) | 0 (0.0) | 0 (0.0) | 1 (0.5) | 1 (12.5) | 5 (12.2) | 3 (2.0) | 9 (4.5) | 21 | 89 | 458 | 568 |

Data are reported as number of patients (%). Percentage values have been calculated after excluding the n for missing values from the denominator.

*BRCA BRCA1 and/or BRCA2; BRCAm BRCA-mutated; BRCAu unknown BRCA status; BRCAwt BRCA wild type; CDK cyclin-dependent kinase; HER2 human epidermal growth factor receptor 2; mBC metastatic breast cancer; PARP poly(ADP-ribose) polymerase; PD-1 programmed cell death protein 1; PD-L1 programmed death-ligand 1; TNBC triple negative breast cancer*
Table S4  Time to first subsequent therapy or death, stratified by either BRCA or HR status

|                  | BRCAm \((n = 72)\) | BRCAwt \((n = 422)\) | BRCAu \((n = 2811)\) | HER2-negative, \((n = 2496)\) | TNBC \((n = 599)\) |
|------------------|---------------------|-----------------------|-----------------------|-----------------------------|---------------------|
| Events, \(n\) (%) | 67 (93.1)           | 359 (85.1)            | 2442 (86.9)           | 2139 (85.7)                 | 545 (91.0)          |
| TFST from date of mBC diagnosis, months, median \((95\% \text{ CI})\) | 7.1 (5.0, 9.2) | 6.9 (6.1, 8.1) | 8.4 (7.9, 9.1) | 9.2 (8.6, 9.9) | 5.4 (5.1, 6.0) |
| TFST from start date of first-line therapy for mBC, months, median \((95\% \text{ CI})\) | 5.1 (3.4, 7.7) | 5.6 (5.1, 6.3) | 6.6 (6.2, 7.0) | 7.2 (6.8, 7.8) | 4.1 (3.7, 4.5) |

*BRCA BRCA1 and/or BRCA2; BRCAm BRCA-mutated; BRCAu unknown BRCA status; BRCAwt BRCA wild type; CI confidence interval; HER2 human epidermal growth factor receptor 2; HR hormone receptor; mBC metastatic breast cancer; TFST time to first subsequent therapy or death; TNBC triple negative breast cancer*
Table S5. Overall survival, stratified by either BRCA or HR status

|                  | BRCAm (n = 83) | BRCAwt (n = 460) | BRCAu (n = 3201) | HER2-negative, HR-positive (n = 768) | HER2-negative, HR-positive (n = 2738) |
|------------------|----------------|------------------|------------------|-------------------------------------|--------------------------------------|
| Events, n (%)    | 44 (53.0)      | 238 (51.7)       | 1996 (62.4)      | 1580 (57.7)                         | 557 (72.5)                           |
| Real-world OS    |                |                  |                  |                                     |                                     |
| from date of mBC | 31.5           | 34.7             | 27.6             | 34.3                                | 12.0                                 |
| median (95% CI)  | (23.1, 42.8)   | (28.9, 44.5)     | (26.1, 29.5)     | (32.7, 36.4)                        | (11.0, 13.3)                         |

BRCA BRCA1 and/or BRCA2; BRCAm BRCA-mutated; BRCAu unknown BRCA status; BRCAwt, BRCA wild type; CI confidence interval; HER2 human epidermal growth factor receptor 2; HR hormone receptor; mBC metastatic breast cancer; OS overall survival; TNBC triple negative breast cancer