Electronic supplementary materials

Breast Cancer

Prevalence of mutations in BRCA and homologous recombination repair genes and real-world standard of care of Asian patients with HER2-negative metastatic breast cancer starting first-line systemic cytotoxic chemotherapy: subgroup analysis of the global BREAKOUT study

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### List of participating institutions

| Country | Institution                                                                 | Number of consented patients |
|---------|-----------------------------------------------------------------------------|------------------------------|
| Japan   | Kitano Hospital, The Tazuke Kofukai Medical Research Institute, Osaka       | 3                            |
| Japan   | NHO Hokkaido Cancer Center, Sapporo                                        | 8                            |
| Japan   | Tohoku University Hospital, Sendai                                          | 6                            |
| Japan   | St. Luke's International Hospital, Tokyo                                     | 4                            |
| Japan   | NHO Shikoku Cancer Center, Matsuyama                                        | 12                           |
| Japan   | NHO Kyushu Cancer Center, Fukuoka                                           | 4                            |
| Japan   | Tesshokai Kameda General Hospital, Kamogawa                                  | 8                            |
| S Korea | Ulsan University Hospital, Ulsan                                             | 10                           |
| S Korea | Asan Medical Center, Seoul                                                   | 7                            |
| S Korea | National Cancer Center, Goyang                                               | 5                            |
| S Korea | Seoul National University Bundang Hospital, Seongnam                         | 6                            |
| S Korea | Severance Hospital, Yonsei University Health System, Seoul                  | 5                            |
| S Korea | Seoul National University Hospital, Seoul                                     | 3                            |
| S Korea | Gangnam Severance Hospital, Yonsei University Health System, Seoul          | 5                            |
| S Korea | CHA Bundang Medical Center, CHA University, Seongnam                         | 3                            |
| S Korea | Dong-A University Hospital, Busan                                            | 4                            |
| S Korea | Chung-Ang University Hospital, Seoul                                          | 2                            |
| Taiwan  | Changhua Christian Hospital, Changhua                                        | 1                            |
| Taiwan  | Chi Mei Medical Center, Tainan                                               | 5                            |
| Taiwan  | China Medical University Hospital, Taichung                                   | 1                            |
| Taiwan  | Kaohsiung Veterans General Hospital, Kaohsiung                               | 3                            |
| Taiwan  | Tri-Service General Hospital, Taipei                                         | 4                            |
| Taiwan  | National Cheng Kung University Hospital, Tainan                              | 2                            |
| Taiwan  | E-Da Hospital, Kaohsiung                                                     | 1                            |
| Taiwan  | Cheng-Hsin Rehabilitation Medical Center, Taipei                             | 4                            |
**Supplemental Tables**

**Supplemental Table 1** Classification of gBRCA mutation results

| BRCA status               | Prior BRCA test results | Baseline gBRCA results* |
|---------------------------|-------------------------|-------------------------|
| Positive gBRCA mutation   | BRCA1m                  | • Deleterious mutation  |
|                           | and/or BRCA2m           | • Genetic variant, suspected deleterious |
|                           |                         | • gBRCA mutation type (classified as gBRCA1 and/or gBRCA2) |
| No gBRCA mutation         | BRCA wild type          | • No deleterious mutation detected |
|                           |                         | • No mutation detected |
|                           |                         | • Genetic variant, favor polymorphism |
|                           |                         | • Genetic variant of uncertain significance |
|                           |                         | • BRCA wild type |

*If the mutation status could not be determined from the blood sample, the results were classified as not determined gBRCA status.
### Supplemental Table 2  
Treatment history prior to diagnosis of metastatic disease in the Asian cohort (full analysis set)

|                                   | Overall (N = 104) | gBRCA1/2m- positive (N = 11) | gBRCA1/2m-negative (N = 93) |
|-----------------------------------|-------------------|------------------------------|-----------------------------|
| Chemotherapy prior to metastatic  | 57 (56.4)         | 7 (63.6)                     | 50 (55.6)                   |
| (n = 101)                         | (n = 11)          |                              | (n = 90)                    |
| Time from end of most recent      | 29.5 (1.1–354.6)  | 30.7 (10.7–176.8)            | 28.2 (1.1–354.6)            |
| chemotherapeutic agent to         | (n = 54)          | (n = 7)                      | (n = 47)                    |
| enrollment, months                |                   |                              |                             |
| Number of cycles of most recent   | 4.0 (1–21)        | 4.0 (3–8)                    | 4.0 (1–21)                  |
| chemotherapeutic agent            | (n = 55)          | (n = 7)                      | (n = 48)                    |
| Chemotherapeutic agents<sup>a,b</sup> | n = 189           | n = 27                       | n = 162                     |
| Cyclophosphamide                  | 57 (30.2)         | 8 (29.6)                     | 49 (30.2)                   |
| Docetaxel                         | 32 (16.9)         | 3 (11.1)                     | 29 (17.9)                   |
| Doxorubicin                       | 28 (14.8)         | 3 (11.1)                     | 25 (15.4)                   |
| 5-fluorouracil                    | 27 (14.3)         | 5 (18.5)                     | 22 (13.6)                   |
| Epirubicin                        | 23 (12.2)         | 4 (14.8)                     | 19 (11.7)                   |
| Non-chemotherapeutic agents prior | 43 (42.2)         | 4 (36.4)                     | 39 (42.9)                   |
| to metastatic disease            | (n = 102)         | (n = 11)                     | (n = 91)                    |
| Time from end of most recent      | 12.5 (0.9–156.6)  | 3.0 (1.1–156.6)              | 12.6 (0.9–92.8)             |
| non-chemotherapeutic agent to     | (n = 38)          | (n = 3)                      | (n = 35)                    |
| enrollment, months                |                   |                              |                             |
| Non-chemotherapeutic agents<sup>a,b</sup> | n = 58           | n = 4                        | n = 54                      |
| Tamoxifen                         | 26 (44.8)         | 3 (75.0)                     | 23 (42.6)                   |
| Letrozole                          | 17 (29.3)         | 1 (25.0)                     | 16 (29.6)                   |
| Anastrozol                        | 7 (12.1)          | 0                            | 7 (13.0)                    |

Values presented are median (range) or n (%).

The number of patients with available data is given where it differs from the overall number of patients. Percentages are based on the number of patients with available data.
a Patients may have received more than one agent

b Agents used in >10% of patients are shown
Supplemental Table 3 Treatments received during metastatic disease prior to first-line chemotherapy in the Asian cohort (full analysis set)

| Treatment                          | Overall (N = 104) | gBRCA1/2 positive (N = 11) | gBRCA1/2 negative (N = 93) |
|------------------------------------|-------------------|---------------------------|---------------------------|
| Use of a non-chemotherapeutic agent before first-line chemotherapy | 42 (40.4)         | 5 (45.5)                  | 37 (39.8)                 |
| Time from end of most recent non-chemotherapeutic agent to enrollment, months | 1.0 (–6.9 to 4.6) | 0.3 (0.3 to 0.3)          | 1.1 (–6.9 to 4.6)         |
| (n = 29)                           | (n = 1)           | (n = 28)                  |                           |
| Non-chemotherapeutic agent<sup>a,b</sup> | n = 101           | n = 14                    | n = 87                    |
| Letrozol                           | 18 (17.8)         | 1 (7.1)                   | 17 (19.5)                 |
| Bevacizumab                        | 15 (14.9)         | 4 (28.6)                  | 11 (12.6)                 |
| Exemestane                         | 14 (13.9)         | 1 (7.1)                   | 13 (14.9)                 |
| Fulvestrant                        | 14 (13.9)         | 2 (14.3)                  | 12 (13.8)                 |
| Everolimus                         | 13 (12.9)         | 1 (7.1)                   | 12 (13.8)                 |

Values presented are median (range) or n (%).

The number of patients with available data is given where it differs from the overall number of patients. Percentages are based on the number of patients with available data.

<sup>a</sup>Patients may have received more than one agent

<sup>b</sup>Agents used in >10% of patients are shown
Supplemental Table 4  First-line systemic cytotoxic chemotherapy for metastatic breast cancer in the Asian cohort (full analysis set)

|                  | Overall (N = 104) | gBRCA1/2m- positive (N = 11) | gBRCA1/2m- negative (N = 93) |
|------------------|-------------------|-----------------------------|-----------------------------|
| Number of unique chemotherapeutic agents taken |                   |                             |                             |
| 1                | 60 (57.7)         | 4 (36.4)                    | 56 (60.2)                   |
| 2                | 38 (36.5)         | 6 (54.5)                    | 32 (34.4)                   |
| 3                | 4 (3.8)           | 0                           | 4 (4.3)                     |
| 4+               | 2 (1.9)           | 1 (9.1)                     | 1 (1.1)                     |
| First-line chemotherapeutic agent<sup>a,b</sup> |                   |                             |                             |
| Paclitaxel       | 32 (30.8)         | 5 (45.5)                    | 27 (29.0)                   |
| Capecitabine     | 24 (23.1)         | 2 (18.2)                    | 22 (23.7)                   |
| Bevacizumab      | 14 (13.5)         | 4 (36.4)                    | 10 (10.8)                   |
| Cyclophosphamide | 13 (12.5)         | 2 (18.2)                    | 11 (11.8)                   |
| Docetaxel        | 11 (10.6)         | 2 (18.2)                    | 9 (9.7)                     |

Values presented are median (range) or n (%).

The number of patients with available data is given where it differs from the overall number of patients. Percentages are based on the number of patients with available data.

<sup>a</sup>Patients may have received more than one agent

<sup>b</sup>Agents used in >10% of patients are shown