Impact of germline BRCA mutations and characteristics patterns on clinical care among women with early breast cancer: an analysis of the prospective CANTO cohort

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Background and study rationale
Germline mutations in BC susceptibility genes and family genetics, such as BRCA1 or BRCA2 are among the well-known risk factors for the development of BC development. 5-30% of BC cases are associated with a germline BRCA mutation (gBRCA), which can impact tumor characteristics and management of the associated BC.

Limited epidemiological data exist in the natural history of the gBRCA disease subtype, and the standard care of treatments used, particularly in the early BC (EC) indication in Europe. Using this prospective ongoing CANTO cohort (Cancer TDCirop; NCT01934398), we conducted a retrospective analysis focusing on clinical characteristics and patterns of care of eBC by gBRCA status.

CANTO is a prospective longitudinal cohort started in 2012 in 26 French comprehensive cancer centers sponsored by UNICANCER. Patients will be followed up for 10 years.

Patients 18+ years old with early stage (stage I-IIIA), untreated invasive BC (including primary surgical care) were included.

Patients were excluded if they had experienced local recurrence of BC or had history of another cancer within 3 years prior to study.

In the present BRCA study 9188 women included from 2012 to 2017 were analyzed by gBRCA status obtained on routine practice. Brca2 mutation (patients with gBRCA mutated status), gBRCA/cut (patients with gBRCA wild type or unknown status).

Study design and statistical analyses
Demographics, medical and family history, disease characteristics and BC treatment were examined overall and per subgroup populations: HER2- (✓/− tested, HER2−/HER2−, HER2+/HER2−, HER2+/HER2+ further segregated by gBRCA status.

Statistical analyses were performed using the SAS statistical software version 9.4. Continuous variables were described as mean, standard deviation, median and range.

Categorical variables were described as frequency and percentage (with 95% Cl or Cerrits-Commenter interval (CI)) of each modality. Percentages were calculated on complete data. The number of missing data was described.

Characteristics of gBRCA patients

In the cohort, 169 women (1.8%) had a gBRCA (92 gBRCA1m and 77 gBRCA2m), 2216 (28.0%) were HER2−/HER2− type (wt) and 6573 (70.2%) gBRCA unknown (uk).

Women with gBRCA were younger than gBRCAwt or uk (mean age 43.7 years [95% CI: 42.0-45.4] versus 53.2 [52.4-54.1] vs 58.2 [57.9 - 58.5] respectively) at BC diagnosis.

The overall median age of diagnosis was 35.0 [30.5-37.3] years.

Characteristics of patients with BRCA mutations were compared to gBRCAwt and/or gBRCA uk.

40 years old and less

54.0 (27.3-52.8) vs 6.4 (5.8-6.0); p<0.0001

Between 40 and 50 years old

60.2 (22.7-63.7) vs 22.6 (21.7-23.4); p<0.0001

Between 50 and 70 years old

51.9 (28.9-57.8) vs 11.9 (11.9-12.7); p<0.0001

More than 70 years old

51.6 (1.6-13.0) vs 12.7 (11.6-13.0); p<0.0001

Tumour characteristics

Consistent with existing literature, higher proportion of triple negative (TN) subtype were observed in the gBRCA women (44% [36.7-52.2] vs gBRCAwt and gBRCAuk 9.5% [8.9-10.1]).

Pathological complete response

We also assessed the rate of pathologic complete response (pCR) to neoadjuvant therapy (defined as no residual invasive disease in the breast and the axillary lymph nodes) based on the Sataloff Classification. On the whole pCR rates were 54.0% (39.3-68.2) in gBRCAwt vs 34.9% (31.9-38.0) in gBRCA uk.

Treatment patterns

gBRCA pts were more likely to undergo radical mastectomy (46.2% [35.0-50.4] vs 23.2 [22.4-24.1]) with more axillary dissection (51.5% [43.5-59.2] vs 32.6 [33.4-33.9]) compared to gBRCAwt and uk pts.

gBRCA pts were also more like to receive chemotherapy 92.9% [87.9-96.3] vs 51.4 [50.4-52.4] especially in the neo adjuvant setting (39.1% [31.6-46.8] vs 12.9 [12.2-13.6]).

Tumours of pts with gBRCA were characterized by higher stage IIIa (65.1% [57.4-72.2] vs 49.8% [48.3-51.5] and histological grade 3 (57.9% [50.4-64.2] vs 26.7 [25.8-28.5]) when compared to gBRCA wt and uk pts.

In our cohort, 30% of eBC pts had their gBRCA status tested; of them 7.1% had a gBRCA mutation.

- Consistent with prior research, women with gBRCA had a substantial proportion of higher stage TN tumours and were treated with more aggressive treatments. They were also more likely to receive radical mastectomy and achieved a higher rate of pCR following receipt of neoadjuvant therapy.

- Further studies on clinical outcomes of eBC pts with gBRCA are warranted in order to assess DFS, OS (survival outcome) and quality of life.

Conclusions

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