A STUDY OF TRIPLE-NEGATIVE BREAST CANCER PATIENTS TESTED WITH A 25-GENE PANEL OF HEREDITARY CANCER GENES

METHODS

Genetic Testing

We queried a commercial laboratory database for patients affected with breast cancer who were tested with a 25-gene panel of hereditary cancer genes from September 2013 through March 2015. Patients affected with TNBC were analyzed separately.

All patient data was obtained by health care provider report on test requisition.

We identified 3,413 patients with a personal history of TNBC and 22,890 patients with a personal history of other breast cancers (49.8).

The mean age-at-diagnosis for patients with TNBC with a pathogenic variant (50.3) was similar to that in patients with other breast cancers (52.2). Patients with TNBC who were of the following ancestries had statistically significant higher positive mutation rates compared to non-TNBC (Figure 1):

- Central/Eastern European: 23.8% (21.2%, 26.4%) vs 18.0% (16.6%, 20.3%)
- Western/Northern European: 13.8% (12.1%, 15.6%) vs 9.3% (8.8%, 9.8%)
- Latin American/Caribbean: 19.1% (14.3%, 24.6%) vs 11.0 (9.5%, 12.7%)

The mean age-at-diagnosis for patients with TNBC with a pathogenic variant (50.3) was similar to that in patients with other breast cancers (49.8).

As previously reported, the TNBC mutation carriers were found to have a higher occurrence of BRCA1 mutations than patients with other breast cancers (50.3% and 18.2%, respectively) (Figure 2).

In line with more recent studies, we also found that 19.3% (99) of mutations in TNBC patients were in BRCA2 (Figure 2).

Additionally, patients with TNBC showed a statistically significant difference in mutation prevalence in several genes relative to patients with other breast cancers (Figure 3):

- Higher prevalence in TNBC:
  - CDH1: 0.4% (0.3%, 0.7%) vs 0.2% (0.1%, 0.3%)
  - RAD51C: 0.3% (0.3%, 0.7%) vs 0.1% (0.1%, 0.2%)
  - PALB2: 1.5% (1.1%, 2.0%) vs 0.8% (0.7%, 1.0%)
- Lower prevalence in TNBC:
  - ATM: 0.1% (0.1%, 0.5%) vs 1.1% (1.0%, 1.2%)
  - CHEK2: 0.2% (0.1%, 0.4%) vs 1.4% (1.2%, 1.5%)

We also found that 10% of patients with TNBC had mutations in two genes, which may allow affected patients to receive more appropriate medical management.

Three additional genes, ATM, BRIP1, and CHEK2, were significantly more prevalent in patients with TNBC compared to patients with other types of breast cancer, while ATM and CHEK2 were significantly less prevalent.

This data offers insight into the underlying genetic mutations that may drive the development of TNBC, which may affect those patients with specific etiologic subtypes.

RESULTS

In all patients with breast cancer, panel testing identified 100.8% more mutations than BRCA1 and BRCA2 testing alone.

- The increase in mutations identified was 43.7% in patients with TNBC and 121.8% in patients with other types of breast cancer.
- The overall mutation prevalence in patients with TNBC was 14.7%, compared to 9.2% in patients with other types of breast cancer.
- The TNBC panel increased the prevalence of mutations in patients with TNBC by 150.8%, compared to patients with other types of breast cancer.

CONCLUSIONS

- The statistically significant increased prevalence of mutations in patients with TNBC, particularly in RAD51C and PALB2, may support targeted clinical action.

Figure 1. Percentage of Patients with TNBC (n=503) and non-TNBC (n=2,095) with a Pathogenic Mutation according to Ancestry

Figure 2. Distribution of Mutations in Patients with (A) TNBC and (B) Non-TNBC

Figure 3. Mutation Prevalence in patients with TNBC and non-TNBC in BRCA1 and BRCA2 (left) and all other genes (right)

Note: Patients with mutations in two genes are counted twice.

Mutation prevalence in the following genes was statistically different in patients with TNBC versus non-TNBC: BRCA1, ATM, BRIP1, CHEK2, RAD51C, RAD51D, and STK11.

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