



More breakthroughs. More victories.

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BACKGROUND

- Although triple-negative breast cancer (TNBC) accounts for 15% to 20% of all breast cancers diagnosed in the US, its epidemiology is not well understood.
- Previous studies have shown a high incidence of BRCA1 and, more recently, BRCA2 mutations in patients with TNBC.
- As panel testing becomes more prevalent, these studies can be extended to other genes with a known breast cancer risk and improve understanding of the genetic origin of TNBC.
- Here we examined the gene distribution of mutations identified with a 25-gene hereditary cancer panel in patients with TNBC.

METHODS

Genetic Testing

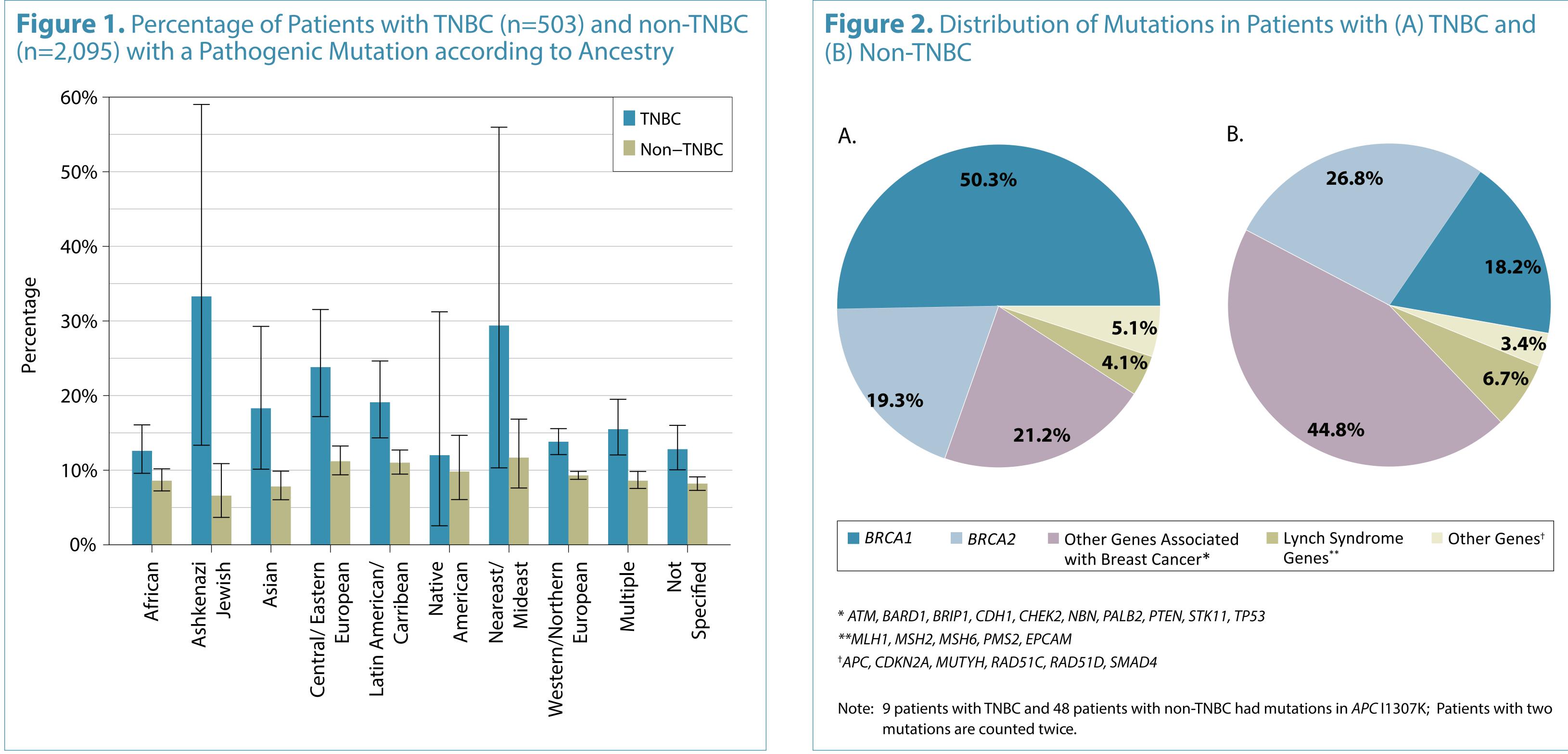
- We queried a commercial laboratory database for patients affected with breast cancer who were tested with a 25-gene panel of hereditary cancer genes from September 2013 through March 2015. Patients affected with TNBC were analyzed separately.
- All patient data was obtained by health care provider report on test requisition forms.
- The panel included BRCA1, BRCA2, TP53, PTEN, MLH1, MSH2, MSH6, PMS2, EPCAM, APC, BMPR1A, CDH1, CDKN2A, MUTYH, SMAD4, STK11, CHEK2, PALB2, ATM, NBN, BARD1, BRIP1, CDK4, RAD51C and RAD51D. Sequencing and large rearrangement was performed for all the genes in the panel (large rearrangement only for EPCAM).
- Only patients with biallelic MUTYH mutations were considered as having a pathogenic *MUTYH* mutation.
- Only results for testing with the full 25-gene panel are shown here. All tests for Ashkenazi Jewish individuals that were initially tested for the 3 common founder mutations in *BRCA1* and *BRCA2* were excluded.

Statistical Methods

Exact confidence intervals (95%) were calculated to identify statistical differences in the positive rate by cancer type (TNBC versus non-TNBC) across ancestry and genes.

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

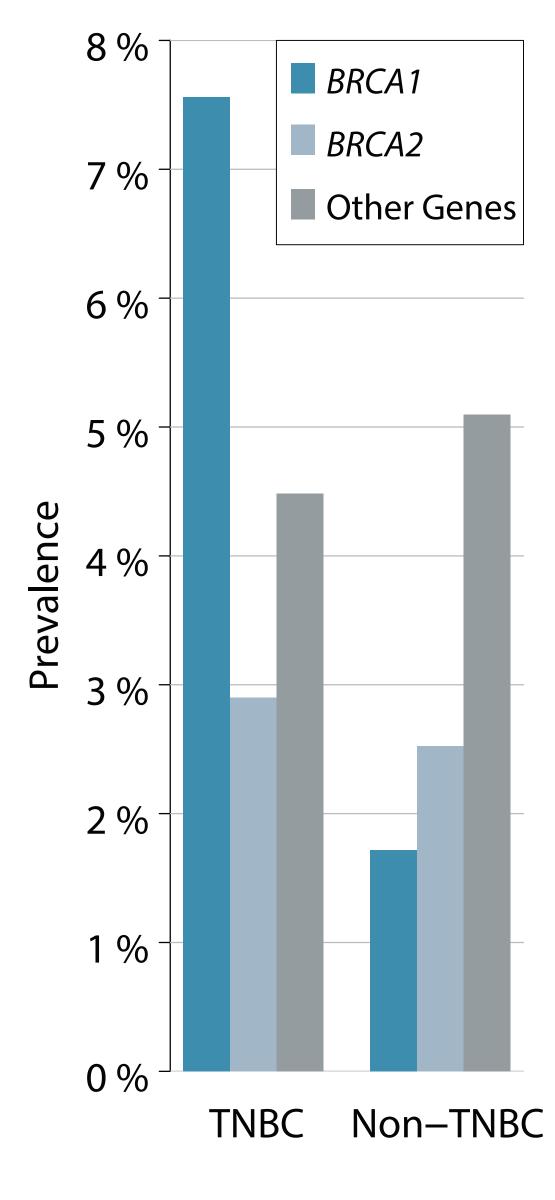
- We identified 3,413 patients with a personal history of TNBC and 22,890 patients with a personal history of other breast cancers.
- Of the TNBC patients, 14.7% (503) were identified as having a pathogenic mutation, compared to 9.2% (2,095) among patients with a personal history of other breast cancers.
- Patients with TNBC who were of the following ancestries had statistically significant higher positive mutation rates compared to patients with non-TNBC (Figure 1):
- Central/Eastern European: 23.8% (17.2%, 31.5%) vs 11.2% (9.4%, 13.2%)
- 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 a 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:
- BARD1: 0.4% (0.3%, 0.7%) vs 0.2% (0.1%, 0.2%)
- *RAD51C*: 0.4% (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: 0.3% (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%)

RESULTS

other genes (right)



Note: Patients with mutations in two genes are counted twice. PALB2, RAD51C.

- testing alone.
- types of breast cancer.
- other types of breast cancer.

Abstract # 1067: For questions regarding this poster, contact John Sandbach: John.Sandbach@USOncology.com.

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

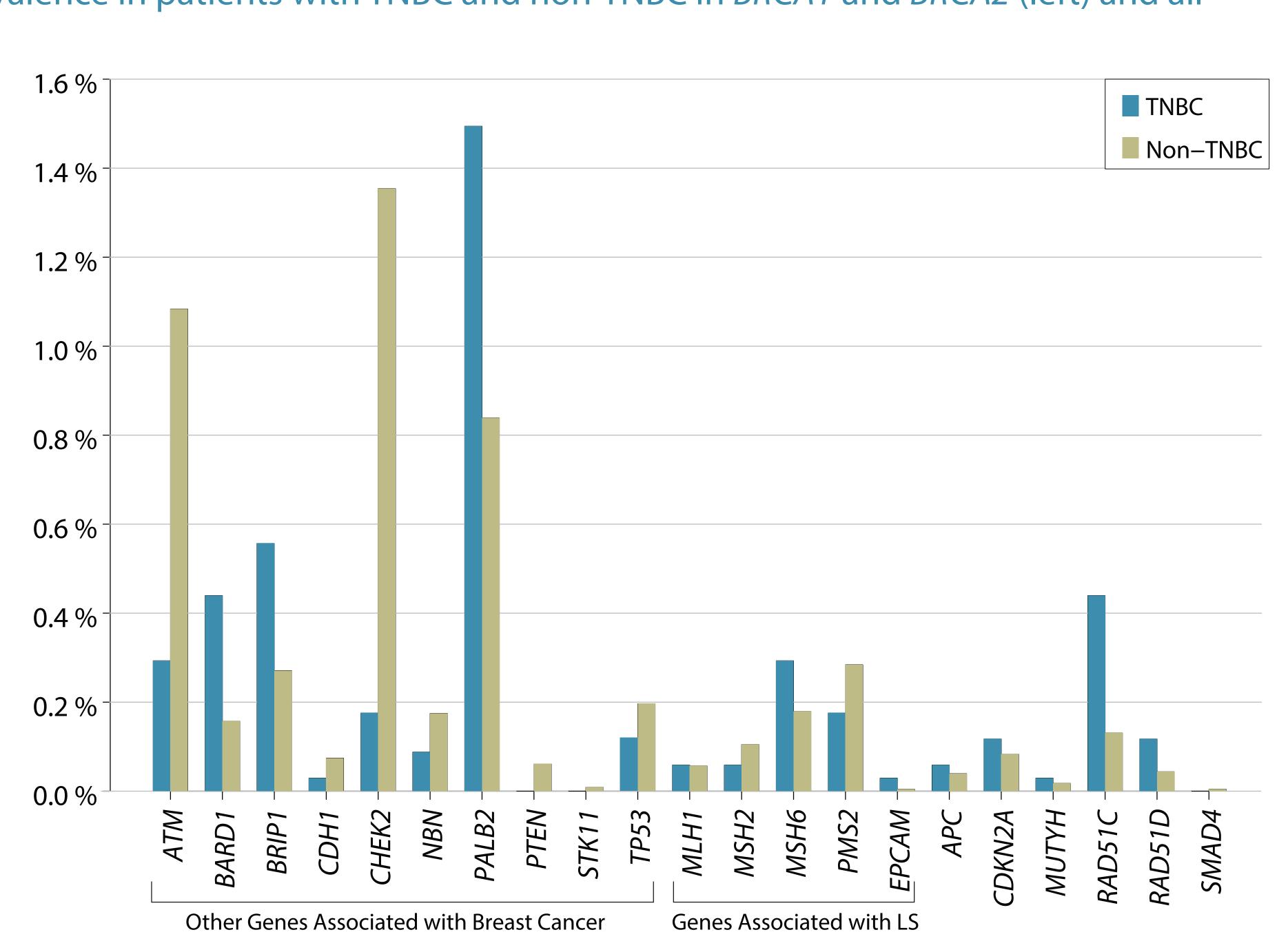


Figure 3. Mutation Prevalence in patients with TNBC and non-TNBC in BRCA1 and BRCA2 (left) and all

Mutation prevalence in the following genes was statistically different in patients with TNBC versus non-TNBC: BRCA1, ATM, BARD1, CHEK2,

CONCLUSIONS

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

• The increase in mutations identified was 43.7% in patients with TNBC and 121.8% in patients with other

The overall mutation prevalence in patients with TNBC was 14.7%, compared to 9.2% in patients with

BARD1, RAD51C, and PALB2 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 allow affected patients to receive more appropriate medical management.