Real-World Outcomes of Germline BRCA-Mutated Triple-Negative Breast Cancer Treated with KEYNOTE-522–Based Neoadjuvant Therapy: Neo-Real/GBECAM-0123 Study

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Introduction

KEYNOTE-522 established pembrolizumab plus neoadjuvant chemotherapy, followed by adjuvant pembrolizumab, as a standard of care in early-stage TNBC.

Germline BRCA-mutated (mBRCA) TNBC represents 10–15% of cases and is characterized by homologous recombination deficiency and high sensitivity to platinum agents and PARP inhibitors.

Real-world data on outcomes of mBRCA TNBC treated with the KEYNOTE-522 regimen remain scarce.

Methods

Design: Multicenter, real-world cohort (Neo-Real/GBECAM-0123).
Population: Consecutive patients with stage II–III TNBC treated according to the KEYNOTE-522 regimen in Brazil and Argentina since July 2020.
BRCA groups: Germline BRCA-mutated (mBRCA) vs germline BRCA wild-type/unknown (wt/unkBRCA).
Primary endpoint: Pathologic complete response (pCR; ypT0/is ypN0).
Secondary endpoints: Event-free survival (EFS) and safety (adverse events, treatment delays, dose reductions, and treatment discontinuations).

Results

Patients: 726 TNBC patients were included; 105 (14.5%) were mBRCA and 621 were wt/unkBRCA.
Baseline characteristics: mBRCA patients were younger (mean 40.2 vs 45.3 years; p<0.001). Stage II disease (73.0% vs 72.3%) and grade 3 tumors (80.2% vs 74.2%) predominated in both groups.
pCR: mBRCA patients achieved higher pCR rates than wt/unkBRCA (74.0% vs 61.4%; p=0.018).
Local treatment: Mastectomy was more frequent in mBRCA (88.3% vs 34.7%; p<0.001), whereas adjuvant radiotherapy was less often used (64.4% vs 87.1%; p<0.001).
Safety: Rates of adverse events, treatment delays, dose reductions, and treatment discontinuations were similar between groups.
EFS: With a median follow-up of 22 months, estimated 3-year event-free survival was ~88% in mBRCA vs ~82% in wt/unkBRCA, with largely overlapping curves and no signal of worse outcomes in the mBRCA group.

Table 1. Comparative Clinical and Treatment Characteristics: mBRCA vs wtBRCA Cohorts

Characteristic	mBRCA (n=105)	wtBRCA (n=621)	p-value / Notes
Median age (years)	40.2	45.3	<0.0001
Premenopausal status	More frequent	Less frequent	—
Clinical stage	Stage II: 72.0% / Stage III: 27.7%	Stage II: 73.0% / Stage III: 27.7%	0.96
Histologic grade 3	76%	69%	0.25
Mean Ki-67 (%)	80%	70%	0.01
Histology: IDC	95%	88%	—
TILs (mean)	15%	15%	—
Neoadjuvant therapy completion	Comparable	Comparable	—
Mastectomy	88.3%	34.7%	<0.001
Adjuvant chemotherapy	3.3%	22.2%	<0.001
Adjuvant immunotherapy (pembrolizumab)	83.3%	78.2%	0.98
Adjuvant radiotherapy	64.4%	76.6%	—

Figure 2. Response to therapy by BRCA status

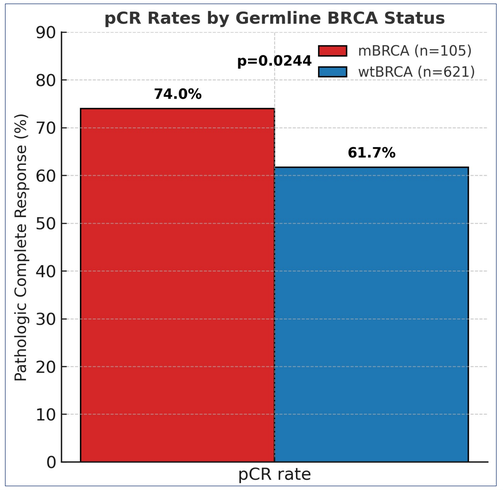
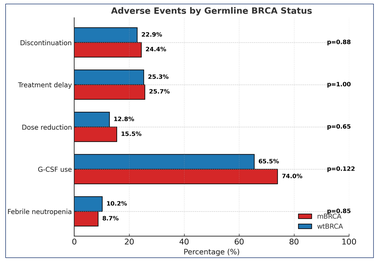


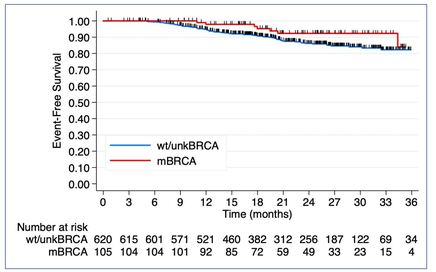
Figure 3. Adverse events according to germline BRCA status.



Conclusion

In this large real-world cohort, germline BRCA-mutated TNBC patients treated with a KEYNOTE-522–based regimen achieved **substantially higher pCR** than wt/unkBRCA patients.
Three-year EFS was high and comparable between groups, with a numerical trend favoring mBRCA, supporting the effectiveness of immunochemotherapy in this biologically distinct subset.
These findings underline the **distinct biology of mBRCA TNBC** and support further research into risk-adapted systemic treatment strategies for hereditary breast cancer.

Figure 4. Event-free survival according to germline BRCA status.



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