Germline BRCA Mutations and Chemo-Immunotherapy Predict Pathologic Complete Response in Triple-Negative Breast Cancer: Insights from a Resource-Limited Setting

Tamer Al-Batsh[1], Faris Tamimi[1],Malek Horani[1], Hira Bani Hani[1], Baha' Sharaf[1],Lulwa EL Saket[1], Mariam Al Atrash[1], Mahmood Abu-Nasser [1], Ahmad Issa[2] , Zaid Muhanna [2], Omar Almuhaisen [2], Hikmat Abdel-Razeq[1 2]
1 King Hussein Cancer Center. Amman, Jordan, 2 School of Medicine, the University of Jordan. Amman, Jordan

Introduction

- Triple-negative breast cancer (TNBC) lacks ER, PR, and HER2 expression, limiting options for targeted therapy.
- Systemic chemotherapy remains the primary treatment approach.[1,2]
- Pathologic complete response (pCR) rates vary widely despite therapeutic advancements.
- Predictive biomarkers are crucial for optimizing treatment selection.
- Chemo-immunotherapy combinations show potential in enhancing pCR outcomes.[3]
- Resource-limited settings face significant challenges in accessing genomic testing and immunotherapy.
- Understanding germline BRCA mutations can help guide treatment Prioritization and inform health policy.[4]
- This study examines the relationship between BRCA mutations and chemo-immunotherapy outcomes in the real-world, resource-limited settings.

Methods and Materials

- This was a retrospective cohort study.
- Included patients diagnosed with TNBC between 2003 and 2023 at King Hussein Cancer Center.
- Demographic, clinical, pathological, and treatment-related data were extracted from medical records.
- All patients underwent germline genetic testing as part of their workup.
- Pathologic complete response (pCR; defined as ypT0/Tis, ypN0), event-free survival (EFS), and overall survival (OS) were estimated using the Kaplan-Meier method.
- Multivariable logistic regression was performed to identify independent predictors of pCR.

Patient Characteristics and Demographics

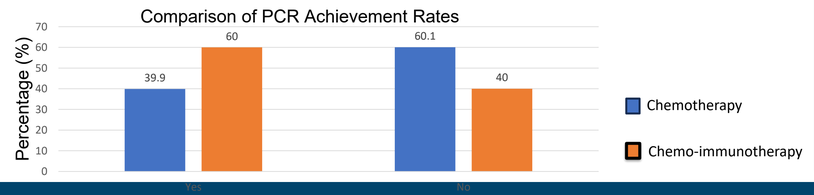
Characteristic	N = 526
Median Age at Diagnosis	**45 (36, 54)**
Gender	
Female	**523 (99.4%)**
Male	**3 (0.6%)**
Stage at Diagnosis	
Metastatic	**32 (6.1%)**
Non-Metastatic	**494 (93.9%)**
Other malignancy (non-breast)	
No	491(93.3%)
yes	35(6.7%)
Family History of malignancy	
Negative	119 (23%)
Positive	407 (77%)
Breast cancer laterality	
Left	269 (51%)
Right	246 (47%)
Bilateral	11 (2%)
Low HER2	95 (18%)

Characteristic	N = 526
Histopathology	
Invasive breast carcinoma of NOS	**507 (96.4%)**
Other	**19 (3.6%)**
Tumor grade	
2	**97 (18%)**
3	**422 (80%)**
Clinical T stage	
T1-T2	**318 (60.4%)**
T3-T4	**166 (31.5%)**
Clinical N stage	
Negative	**238 (45.2%)**
Positive	**259 (49.3%)**
Type of first-line therapy	
Neoadjuvant	338 (68.4%)
Surgery	155 (31.4%)
Did the patient receive immunotherapy as part of neoadjuvant therapy	
No	263(77.8%)
yes	75 (22.2%)

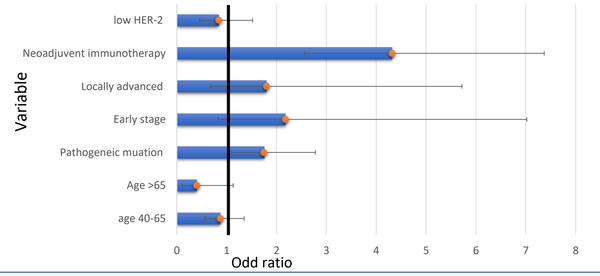
Results

- Among 494 non-metastatic patients, 337 (68.2%) received neoadjuvant therapy, of whom 74 (21.9%) received a combination of chemotherapy and immunotherapy.
- The addition of immunotherapy resulted in a significantly higher pathological complete response (pCR) rate compared to chemotherapy alone (60.1% vs. 39.9%, p < 0.01).

PCR	Chemotherapy alone	Chemotherapy with immunotherapy	P-value
Yes	105/263 (39.9%)	45/75 (60%)	P value <0.01
No	158/263 (60.1%)	30/75 (40%)	

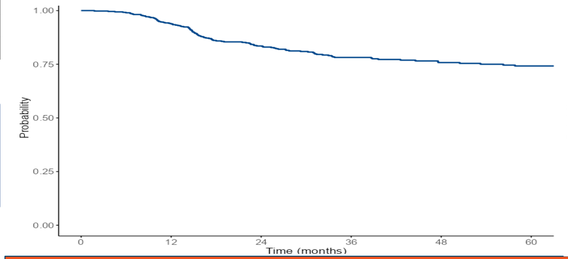


Results

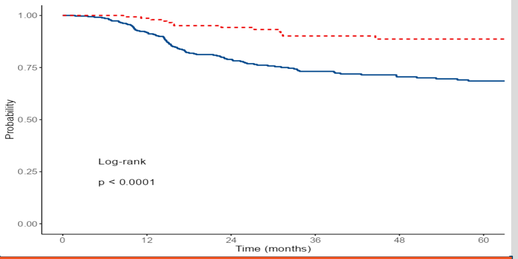


- The most common pathogenic variants were found in BRCA1 (82 cases, 66.1%) and BRCA2 (32 cases, 22.8%).
- Among the 434 patients who underwent multigene panel testing, only 10 (2.3%) carried mutations outside of BRCA1 and BRCA2, with just two involving high-penetrance breast cancer genes (TP53 and PALB2).

EFS for Nonmetastatic Patient



Event-Free Survival According to pCR Status



Conclusions

- Triple-negative breast cancer (TNBC) in Jordan predominantly affects a younger population and is frequently associated with a strong family history of cancer.
- Pathogenic germline variants were identified in 22% of patients, mainly involving BRCA1/2 mutations.[4]
- Patients receiving chemo-immunotherapy demonstrated a significantly higher pathological complete response (pCR) rate compared to chemotherapy alone (59.5% vs. 39.9%; OR = 2.2, p = 0.003).[3,4]
- Both immunotherapy use and the presence of BRCA mutations independently predicted pCR.
- Five-year event-free survival (EFS) was approximately 74%, with no significant difference observed between BRCA-mutated and wild-type groups.
- These findings underscore the value of incorporating immunotherapy into neoadjuvant treatment regimens for TNBC.

Contact :
Tamer Al-Batsh MD
King Hussein Cancer Center
Email: Ta.11015@khcc.jo
Website: www.khcc.jo
Phone: +962 7 9994 01988

References
1. Poggio F, Bruzzone M, Ceppi M, Pondé N, La Valle G, Del Mastro L, et al. Platinum-based neoadjuvant chemotherapy in triple-negative breast cancer: a systematic review and meta-analysis. *Ann Oncol.* 2018;29(7):1497–1508.
2. Jia X, Liu G, Wang C, Zhang W, Jin S, Lou H, et al. Efficacy of platinum-based chemotherapy in triple-negative breast cancer with germline BRCA mutations: a systematic review and meta-analysis. *Breast Cancer Res Treat.* 2022;194(1):1–12.
3. Schmid P, Cortes J, Dent R, Higgins B, Pusztai L, McArthur HL, et al. Event-free survival with pembrolizumab in early triple-negative breast cancer. *N Engl J Med.* 2022;386(6):556–67.
4. Myers SP, Banerjee S, Wei C, Murthy RK, Litton JK, Huo L, et al. Association of germline BRCA pathogenic variants with pathologic complete response after neoadjuvant systemic therapy in triple-negative breast cancer. *NPJ Breast Cancer.* 2024;10:33.

PS4-07-14

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com