PARP Inhibition: Genomics-Informed Care for Patients With Malignancies Driven by *BRCA1*/*BRCA2* Pathogenic Variants

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BACKGROUND: Germline and somatic biomarker testing for *BRCA1/2* pathogenic variants can provide important susceptibility, prognostic, and predictive information, guiding recommendations for care.

OBJECTIVES: This article reviews *BRCA1/2*, DNA damage and repair mechanisms, prevention and screening guidelines for patients with germline pathogenic *BRCA1/2* variants, indications for poly (ADP-ribose) polymerase (PARP) inhibitor therapy, associated side effects, tumor resistance, and implications for nurses.

METHODS: A comprehensive review of the CINAHL®, MEDLINE®, and PubMed® databases was performed using the following search terms: *BRCA1/2*, *PARP inhibitors*, and *genomic testing*.

FINDINGS: PARP inhibitors are indicated for select patients with malignancies associated with *BRCA1/2* pathogenic variants. Awareness of PARP inhibitors, their mechanism of action, indications for use, and associated side effects helps oncology nurses guide patients and families in care recommendations, provide detailed patient education, effectively monitor for side effects, and promote adherence to therapy.

KEYWORDS
genomic science; PARP inhibitor; BRCA1/BRCA2; germline; somatic; biomarkers

DIGITAL OBJECT IDENTIFIER
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GENOMIC SCIENCE HAS EXPANDED THE SCOPE, complexity, and precision of care for patients with cancer. The understanding of specific genetic pathogenic variants, including *BRCA1*/*BRCA2*, has led to updated implications for the prevention, screening, detection, and treatment of certain malignancies. These improvements in the individualization of oncology care delivery present challenges and opportunities for nurses to provide comprehensive care not only for patients but also their families, with the goal of improving outcomes and enhancing quality of life.

The tumor suppressor genes *BRCA1*/*BRCA2* inhibit cell proliferation and tumor development. Pathogenic variants in these genes increase the risk of developing multiple malignancies, have implications for the selection of therapies, and provide some prognostic information. This article reviews the function of *BRCA1*/*BRCA2* genes, relevant DNA repair mechanisms, prevention and screening guidelines for at-risk individuals, indications for poly (ADP-ribose) polymerase (PARP) inhibitor therapy, associated side effects, tumor resistance, and relevant implications for oncology nurses.

BRCA1/BRCA2 Biomarker Testing

Biomarker testing for pathogenic variants, such as in the *BRCA1*/*BRCA2* genes, has revolutionized oncology practice (Mahon, 2020). Biomarker testing can provide valuable information about disease susceptibility, prognosis, and treatment efficacy.

The *BRCA1*/*BRCA2* genes were isolated more than two decades ago, and early research and clinical practice focused on cancer risks associated with germline (inherited) pathogenic variants in these tumor suppressor genes (Petrucelli et al., 2022). A tumor suppressor gene directs the production of a protein, helping to regulate cell division. When the gene is altered, cell division is uncontrolled, ultimately leading to malignancy (Joyce et al., 2022). Therefore, *BRCA1*/*BRCA2* genes are considered susceptibility biomarkers because a pathogenic variant in either gene is associated with an increased risk of developing breast, ovarian, prostate, pancreatic, or malignant melanoma cancer (National Comprehensive Cancer Network, 2023).

BRCA1/*BRCA2* biomarker testing provides prognostic data. Prognostic biomarkers aid in anticipating oncologic outcomes, including disease progression or recurrence (National Library of Medicine, 2016). For example,