Elite Journal of Medicine. Volume 2 issue 2(2024), Pp. 55-66
https://epjournals.com/journals/EJM

BRCA Mastery: Redefining Breast Cancer Care through Cutting-edge Diagnosis and Management

*Emmanuel Ifeanyi Obeagu[1] and Getrude Uzoma Obeagu[2]

[1]Department of Medical Laboratory Science, Kampala International University, Uganda.
[2]School of Nursing Science, Kampala International University, Uganda.

*Corresponding authour: Emmanuel Ifeanyi Obeagu, Department of Medical Laboratory Science, Kampala International University, Uganda.

E-mail: emmanuelobeagu@yahoo.com, obeagu.emmanuel@kiu.ac.ug, 0000-0002-4538-0161

Abstract

The discovery of BRCA mutations has revolutionized the landscape of breast cancer care, offering profound insights into its diagnosis and management. This paper aims to summarize the pivotal role of BRCA mutations in reshaping precision medicine approaches and personalized therapies for breast cancer patients. It explores the significance of genetic testing in identifying BRCA mutations, elucidates their impact on prognosis, and highlights the transformative effects on therapeutic interventions. Furthermore, this paper emphasizes the latest advancements in utilizing BRCA knowledge to tailor patient-specific treatment strategies, underscoring the evolving paradigm of breast cancer care towards individualized precision treatments. Through this exploration, the abstract provides a concise overview of how BRCA mastery is redefining breast cancer care, offering hope for improved patient outcomes and innovative treatment modalities.

Keywords*: BRCA mutations, Breast cancer, Diagnosis, Management, Precision medicine, Therapeutic advancements, Prognosis*

Introduction

Breast cancer remains a significant global health concern, affecting millions of individuals worldwide and posing considerable challenges in diagnosis, treatment, and prognosis.[1-4] Amidst this landscape, the discovery of BRCA mutations has emerged as a groundbreaking milestone, significantly altering our comprehension of breast cancer etiology and treatment strategies.[5] The identification of BRCA1 and BRCA2 genes marked a pivotal moment in oncology, revealing the genetic underpinnings associated with an increased risk of breast and ovarian cancers. These mutations, originally recognized for their hereditary implications, have since evolved into key determinants in the personalized management of breast cancer.[6]

This paper seeks to provide a comprehensive overview of the transformative impact of BRCA mutations on breast cancer care. It explores the journey from the initial discovery of BRCA mutations to their current status as essential markers guiding diagnosis, prognosis, and targeted therapeutic interventions. Furthermore, it elucidates the significance of genetic testing in identifying BRCA mutations and its role in tailoring individualized treatment plans, marking a shift towards precision medicine in breast cancer care.

The genesis of our understanding of hereditary breast cancer can be traced back to the 1990s when pioneering research efforts led to the identification of BRCA1 and BRCA2 genes.[7] In 1994, the landmark discovery of BRCA1 on chromosome 17q21 by a collaborative team led by Dr. Mary-Claire King and colleagues marked a seminal moment in the field of cancer genetics. This groundbreaking finding provided crucial insights into the hereditary nature of certain breast and ovarian cancers. Subsequently, in 1995, researchers identified BRCA2 on chromosome 13q12, further expanding our knowledge of genetic susceptibility to breast cancer. The discovery of these genes shed light on familial clusters of breast cancer and unveiled the intricate genetic mechanisms underpinning the disease.

The recognition of BRCA1 and BRCA2 mutations as major genetic predispositions for breast and ovarian cancers transformed the landscape of cancer research and clinical practice.[6] These findings spurred an era of intensified investigation into the genetic basis of cancer susceptibility, fueling efforts to unravel the complex interplay between inherited genetic factors and cancer development. The identification of BRCA mutations not only provided crucial insights into the molecular pathways involved in tumorigenesis but also facilitated the development of genetic testing methodologies for identifying individuals at heightened risk of hereditary breast cancer. This discovery laid the foundation for a paradigm shift towards personalized medicine, wherein tailored interventions and surveillance strategies could be employed for at-risk individuals.[6]

The significance of BRCA mutations in breast cancer development is profound, as these genetic alterations play a pivotal role in understanding the hereditary basis, risk assessment, and personalized management of this malignancy.[6] BRCA1 and BRCA2 mutations stand as prominent genetic risk factors associated with the development of breast cancer. The presence of these mutations significantly elevates the lifetime risk of developing breast cancer, with BRCA1 mutations conferring a lifetime risk estimated between 60-70%, and BRCA2 mutations increasing the risk to around 50-60%. Compared to the general population, individuals harboring these mutations face a substantially heightened susceptibility to breast cancer onset at a younger age.[8]

Understanding the role of BRCA mutations in breast cancer development has unveiled critical insights into the intricate molecular pathways governing tumorigenesis. Both BRCA1 and BRCA2 genes encode tumor suppressor proteins involved in maintaining genomic stability and orchestrating DNA repair mechanisms within cells. Mutations in these genes compromise their normal function, leading to an impaired ability to repair DNA damage, thus fostering an environment conducive to the accumulation of genetic abnormalities and promoting cancer initiation and progression.[8] Importantly, the inheritance of BRCA mutations follows an autosomal dominant pattern, meaning that individuals carrying a single mutated copy of either BRCA1 or

BRCA2 gene have an increased risk of developing breast cancer. This hereditary predisposition underscores the importance of genetic counseling and testing, allowing for the identification of at-risk individuals within families with a history of breast cancer. Early detection of these mutations enables tailored surveillance strategies and informed decision-making regarding risk-reducing interventions, such as prophylactic surgeries or enhanced screening protocols.[9]

Furthermore, the presence of BRCA mutations has therapeutic implications. Tumors associated with BRCA mutations often display specific vulnerabilities, such as deficiencies in DNA repair mechanisms.[10] Exploiting these vulnerabilities has led to the development of targeted therapies, like PARP inhibitors, which exploit the impaired DNA repair mechanisms in BRCA-mutated cancer cells, leading to their selective destruction.[11-12] The recognition of BRCA mutations as key drivers of hereditary breast cancer has revolutionized risk assessment, genetic screening, and personalized management strategies. By elucidating the genetic underpinnings of breast cancer susceptibility, BRCA mutations have not only facilitated early detection and risk mitigation but have also paved the way for innovative targeted therapies, offering new avenues for treatment and improved outcomes for affected individuals.

BRCA Mutations and Diagnosis

BRCA mutations play a crucial role in the diagnosis of breast cancer, particularly in identifying individuals at an increased risk of hereditary breast cancer. Understanding the significance of these mutations in diagnostic procedures is essential for early detection and personalized management strategies.[6] Genetic testing for BRCA mutations involves analyzing DNA samples obtained from blood or saliva to detect alterations in the BRCA1 and BRCA2 genes.[13] This testing is typically recommended for individuals with a significant family history of breast or ovarian cancer, especially if multiple family members have been diagnosed at a young age or if certain patterns of cancer occurrence exist within the family. Identification of BRCA mutations aids in assessing an individual's risk of developing breast cancer.[14] Positive test results indicate an increased likelihood of developing breast cancer over a lifetime, prompting personalized risk management strategies and heightened surveillance.

BRCA mutation carriers benefit from specialized screening protocols, including more frequent mammograms, breast MRIs, and clinical breast exams, often initiated at an earlier age than standard guidelines recommend for the general population.[15] These intensified surveillance measures aim to detect breast cancer at its earliest stages when treatment options are generally more effective. Positive test results for BRCA mutations have implications for family members. Genetic counseling and testing for at-risk relatives are recommended to identify other individuals who may carry the same mutations, enabling them to make informed decisions regarding their healthcare and risk-reduction options.[7] Knowledge of BRCA mutations may influence treatment decisions. It can guide the selection of therapies, such as PARP inhibitors, which specifically target vulnerabilities in BRCA-mutated cancer cells.[16] Additionally, it may prompt considerations for risk-reducing surgeries or different treatment approaches.

Despite its significance, genetic testing for BRCA mutations has limitations, including the presence of variants of uncertain significance (VUS) and potential psychosocial impacts following positive test results.[17] Additionally, accessibility and affordability of genetic testing pose challenges, limiting its availability to all individuals who may benefit from it. BRCA mutations play a pivotal role in the diagnosis and management of breast cancer. Genetic testing for these mutations enables early identification of individuals at increased risk, facilitating personalized screening, surveillance, and treatment strategies.[6] As research and technology progress, addressing challenges related to testing and expanding access to genetic services will be crucial in optimizing breast cancer diagnosis and management for individuals with BRCA mutations.

BRCA Mutations in Breast Cancer Management

BRCA mutations have substantial implications for the management of breast cancer, influencing treatment decisions, therapeutic approaches, and overall patient care. Understanding the role of these mutations is essential for tailoring personalized strategies in the management of breast cancer patients. Identification of BRCA mutations influences treatment decisions for breast cancer patients. Patients with BRCA mutations may respond differently to various treatment modalities compared to those without these mutations. This knowledge guides oncologists in selecting the most effective therapies while considering the patient's genetic profile. BRCA mutations have paved the way for targeted therapies, such as Poly (ADP-ribose) polymerase (PARP) inhibitors. These drugs exploit the specific vulnerabilities in BRCA-mutated cancer cells, hindering their ability to repair DNA damage and leading to cancer cell death. PARP inhibitors have shown promise in the treatment of BRCA-associated breast cancers, providing a more tailored and effective treatment option.[16]

Breast cancers with BRCA mutations may exhibit increased sensitivity to certain chemotherapy agents.[18] This sensitivity profile may influence the choice and effectiveness of chemotherapy regimens, optimizing treatment outcomes for patients with BRCA-associated breast cancers. BRCA mutations may influence surgical decisions. Some individuals with BRCA mutations may opt for risk-reducing surgeries, such as bilateral mastectomy or oophorectomy, to significantly reduce the risk of developing breast or ovarian cancers, respectively. Additionally, knowledge of BRCA mutations might impact decisions regarding the extent of surgery and reconstruction options after a breast cancer diagnosis. Patients with BRCA mutations benefit from more intensive surveillance measures to detect potential recurrences or new cancer developments.[19] Close monitoring through imaging studies and clinical exams helps in early detection and timely intervention.

BRCA mutations play a crucial role in clinical trial enrollment for novel therapies targeting specific genetic alterations. Participation in trials exploring innovative treatments tailored to BRCA-associated breast cancers offers potential benefits for patients and contributes to advancing the field of oncology.[18] Managing breast cancer in the context of BRCA mutations involves comprehensive counseling and support services. Patients and their families may require guidance in understanding the implications of genetic testing results, treatment decisions, and long-term care planning.[6] BRCA mutations significantly impact the management of breast cancer by influencing

treatment choices, guiding targeted therapies, and shaping surgical and surveillance strategies. Incorporating BRCA-related considerations into personalized treatment plans enhances the quality of care and outcomes for individuals affected by breast cancer. Ongoing research and advancements in precision medicine continue to expand the therapeutic options available for BRCA-associated breast cancers, emphasizing the importance of integrating genetic information into comprehensive patient care.[20-21]

Prognostic Significance of BRCA Mutations

The prognostic significance of BRCA mutations in breast cancer is an area of substantial interest and ongoing research.[22] Understanding the impact of these mutations on disease prognosis is crucial in guiding treatment decisions and predicting patient outcomes. Studies investigating the prognostic implications of BRCA mutations in breast cancer have reported varied findings.[23-24] Some research suggests that BRCA-associated breast cancers may exhibit unique clinical characteristics, such as a higher likelihood of being triple-negative (lacking estrogen receptors, progesterone receptors, and HER2/neu expression) and displaying specific pathological features. These cancers may respond differently to treatments, impacting survival rates and outcomes.[25-26]

While some studies suggest that BRCA mutations are associated with a more aggressive tumor phenotype and poorer outcomes due to their high-grade nature and potential resistance to certain therapies, other research indicates comparable or even better survival rates in BRCA mutation carriers after adjusting for various factors.[27-28] These discrepancies highlight the complexity of interpreting the prognostic implications of BRCA mutations and the need for further investigation. The presence of BRCA mutations may influence the response to specific therapies.[29] For instance, BRCA-associated breast cancers might exhibit increased sensitivity to certain chemotherapy agents or targeted therapies like PARP inhibitors. The differential response to treatments based on the presence of BRCA mutations can impact disease progression and overall survival.

Breast cancers associated with BRCA mutations often present at a younger age compared to sporadic cases.[30] The age of onset might influence the disease course and response to treatment, potentially affecting long-term outcomes. Despite extensive research, the exact prognostic implications of BRCA mutations in breast cancer remain inconclusive in certain aspects. Studies with larger sample sizes and longer follow-up periods are warranted to elucidate the precise impact of these mutations on disease progression, survival rates, and treatment responses. Furthermore, investigating the interplay between BRCA mutations and other genetic or environmental factors could provide a more comprehensive understanding of their prognostic significance.

Therapeutic Advancements and Future Directions

Therapeutic advancements in the context of BRCA-associated breast cancer have shown promising strides, especially with the emergence of targeted therapies.[30] Looking ahead, future directions in this field aim to further refine treatment approaches, expand therapeutic options, and optimize outcomes for patients with BRCA mutations. The development of PARP inhibitors represents a significant therapeutic advancement for BRCA-associated breast cancer.[32] These inhibitors exploit

the vulnerabilities in DNA repair mechanisms specific to BRCA-mutated cancer cells, leading to their selective destruction. Continued research focuses on refining the use of PARP inhibitors and exploring their efficacy in different disease stages and in combination with other treatment modalities.

Investigations into immunotherapeutic approaches for breast cancer, including immune checkpoint inhibitors, are ongoing. Understanding the immune microenvironment of BRCA-mutated tumors and exploring immunomodulatory agents may offer novel treatment avenues and improve responses in these specific subtypes of breast cancer. Identifying additional predictive biomarkers beyond BRCA mutations could refine patient selection for targeted therapies.[33] Biomarkers associated with treatment response or resistance to specific agents may assist in personalizing treatment strategies further. Ongoing and future clinical trials continue to explore innovative treatment modalities and combinations tailored to BRCA-associated breast cancers. These trials aim to assess the efficacy and safety of novel agents, refine treatment protocols, and improve patient outcomes. Advancements in risk-reducing strategies for individuals with BRCA mutations are a focus for future research. This includes evaluating the effectiveness of preventive interventions, such as chemoprevention, lifestyle modifications, and risk-reducing surgeries, in reducing cancer incidence and improving overall health outcomes. The evolving landscape of precision medicine emphasizes individualized treatment approaches based on a patient's unique genetic profile. Future directions in BRCA-associated breast cancer care involve tailoring therapies to specific genetic alterations, optimizing treatment responses, and minimizing adverse effects.

Therapeutic advancements in BRCA-associated breast cancer, particularly with targeted therapies like PARP inhibitors, have shown promise in improving outcomes for affected individuals.[32] Future directions focus on further refining treatment strategies, exploring novel therapeutic avenues, integrating predictive biomarkers, and advancing personalized care approaches. Continued research efforts and participation in clinical trials will drive the evolution of treatment paradigms, ultimately aiming to enhance the quality of care and outcomes for patients with BRCA mutations and breast cancer.

Challenges and Opportunities

Addressing the challenges and leveraging opportunities in the context of BRCA-associated breast cancer care is crucial for advancing research, improving patient outcomes, and ensuring equitable access to optimal healthcare interventions.

Challenges:

Limited access to genetic testing remains a significant challenge, preventing some individuals at risk of carrying BRCA mutations from obtaining essential information about their genetic predisposition to breast cancer.[34] Cost, insurance coverage, and availability of genetic counseling services can pose barriers to widespread testing. Variants of uncertain significance (VUS) detected during genetic testing present challenges in clinical decision-making.[35] These ambiguous findings

complicate risk assessment and necessitate continuous research and updated databases to refine the interpretation of these variants. The implications of genetic testing results, especially positive findings for BRCA mutations, can have profound psychological impacts on individuals and their families.[36] Ethical considerations surrounding issues like privacy, genetic discrimination, and psychological support for patients and their relatives are critical aspects that need attention. Despite the efficacy of targeted therapies like PARP inhibitors, the development of resistance mechanisms remains a challenge. Tumor cells may adapt, leading to treatment resistance and disease relapse, highlighting the need for alternative strategies and combination therapies.[32]

Opportunities:

Rapid advancements in genetic sequencing technologies and research methodologies present opportunities for refining our understanding of BRCA mutations' biological implications. These advancements can aid in identifying new therapeutic targets and predicting treatment responses more accurately.[37-38] The paradigm of precision medicine offers opportunities to tailor treatments based on an individual's genetic profile. Continued research into targeted therapies and biomarkers specific to BRCA-associated breast cancers provides avenues for personalized treatment approaches. Collaborative efforts among researchers, clinicians, pharmaceutical companies, and patients in conducting clinical trials are essential. Participation in trials exploring novel therapeutic agents and treatment combinations contributes to advancing knowledge and improving patient care. Education initiatives and advocacy efforts aimed at raising awareness about BRCA mutations, risk assessment, genetic testing, and available resources play a vital role. Increasing public and healthcare provider awareness can facilitate timely testing, risk reduction, and informed decision-making. Addressing disparities in access to genetic testing, counseling services, and advanced treatments is crucial. Efforts to ensure equitable access to high-quality healthcare interventions for all individuals, regardless of socioeconomic status or geographical location, are imperative.

Recognizing and addressing the challenges while embracing opportunities in BRCA-associated breast cancer care are pivotal in advancing research, improving patient outcomes, and fostering a more comprehensive and equitable healthcare landscape. Collaboration among stakeholders, continued research, ethical considerations, and advocacy efforts are essential for navigating these challenges and maximizing opportunities to benefit individuals affected by BRCA mutations and breast cancer.

Implications for Clinical and Health Policy Making

The implications of BRCA-associated breast cancer for clinical practice and health policy-making are multifaceted, encompassing various aspects of patient care, genetic testing, treatment access, and resource allocation.

Clinical Implications

Incorporating BRCA testing into routine clinical practice allows for risk assessment, early detection, and tailored management strategies for individuals at risk of hereditary breast cancer.

Encouraging healthcare providers to offer genetic counseling and testing to appropriate candidates can identify BRCA mutations and guide personalized patient care. Knowledge of BRCA mutations informs treatment decisions, guiding the selection of targeted therapies and tailored interventions for patients with BRCA-associated breast cancers. Integrating genetic information into treatment planning enhances treatment efficacy and improves patient outcomes. Identifying individuals with BRCA mutations enables the implementation of risk-reducing interventions, such as enhanced surveillance, chemoprevention, or risk-reducing surgeries. Healthcare providers can offer guidance and support to individuals in making informed decisions about preventive measures. Individuals with BRCA mutations benefit from specialized surveillance measures and early detection strategies. Regular screenings, including imaging studies and clinical exams, aid in timely detection of breast cancer or precancerous lesions, potentially improving treatment outcomes.[38-43]

Health Policy Implications

Health policies that promote increased access to genetic testing, such as insurance coverage for testing and counseling services, reduce financial barriers and ensure equitable access to essential healthcare services for individuals at risk of carrying BRCA mutations. Health policy initiatives focusing on educating healthcare providers about the significance of BRCA mutations, guidelines for genetic testing, and the interpretation of results are essential. Training programs can facilitate the integration of genetic information into clinical practice. Policies supporting research initiatives focused on BRCA-associated breast cancer, including clinical trials investigating novel therapies and predictive biomarkers, foster advancements in treatment options and improved patient care. Health policies addressing ethical issues related to genetic testing, including privacy, informed consent, and protection against genetic discrimination, ensure ethical standards are upheld in clinical practice. Policies that support patient advocacy groups and support networks for individuals and families affected by BRCA mutations can enhance awareness, access to resources, and emotional support. Integrating BRCA-associated breast cancer considerations into clinical practice and health policy-making involves promoting access to genetic testing, guiding personalized treatment approaches, ensuring ethical standards, and advocating for patient support. A comprehensive approach that considers both clinical needs and health policy initiatives is essential for optimizing care and improving outcomes for individuals with BRCA mutations and breast cancer.[44-45]

Conclusion

The discovery and understanding of BRCA mutations have fundamentally transformed the landscape of breast cancer diagnosis, treatment, and management. The implications of BRCA mutations in clinical practice, research, and health policy-making are extensive and far-reaching, offering both challenges and opportunities in the quest to improve patient outcomes. Moving forward, collaborative efforts among healthcare providers, researchers, policymakers, patient advocates, and the broader community are essential. Emphasizing education, expanding access to genetic testing, advancing research, and addressing ethical considerations will be pivotal in navigating the complexities associated with BRCA mutations in breast cancer.

The evolving landscape of BRCA-associated breast cancer care necessitates a holistic approach, encompassing precision medicine, ethical guidelines, equitable healthcare access, and continuous research endeavors. By addressing these multifaceted aspects, we can strive towards improved patient care, enhanced outcomes, and a more equitable healthcare environment for individuals affected by BRCA mutations and breast cancer. Ultimately, the ongoing commitment to research, advocacy, and patient-centered care remains crucial in the journey to redefine breast cancer management and ensure better prospects for those impacted by this disease.

References

1. Obeagu EI, Babar Q, Vincent CC, Udenze CL, Eze R, Okafor CJ, Ifionu BI, Amaeze AA, Amaeze FN. Therapeutic targets in breast cancer signaling: A review. Journal of Pharmaceutical Research International. 2021;33(56A):82-99.
2. Obeagu EI, Ahmed YA, Uzoma G. Biomakers of breast cancer: Overview. **Int. J. Curr. Res. Biol. Med. (2023). 8(1): 8-16**
3. Obeagu EI, Muhimbura E, Kagenderezo BP, Nakyeyune S, Obeagu GU. An Insight of Interleukin-6 and Fibrinogen: In Regulating the Immune System. J Biomed Sci. 2022;11(10):83.
4. Obeagu EI, Babar Q, Vincent CC, Anyanwu CO, Uduchi IO. Advances in Therapeutic Strategies of Immunotherapy in Cancer Treatment. World Journal of Pharmacy and Pharmaceutical Sciences. 2021;10(8):2144-64.
5. Yeoh KG, Tan P. Mapping the genomic diaspora of gastric cancer. Nature reviews cancer. 2022;22(2):71-84.
6. Nielsen SM, Eccles DM, Romero IL, Al-Mulla F, Balmaña J, Biancolella M, Blok R, Caligo MA, Calvello M, Capone GL, Cavalli P. Genetic testing and clinical management practices for variants in non-BRCA1/2 breast (and breast/ovarian) Cancer susceptibility genes: an international survey by the evidence-based network for the interpretation of Germline mutant alleles (ENIGMA) clinical working group. JCO precision oncology. 2018; 2:1-42.
7. Turnbull C, Rahman N. Genetic predisposition to breast cancer: past, present, and future. Annu. Rev. Genomics Hum. Genet. 2008; 9:321-45.
8. Mahdavi M, Nassiri M, Kooshyar MM, Vakili-Azghandi M, Avan A, Sandry R, Pillai S, Lam AK, Gopalan V. Hereditary breast cancer; Genetic penetrance and current status with BRCA. Journal of cellular physiology. 2019;234(5):5741-50.
9. Mehrgou A, Akouchekian M. The importance of BRCA1 and BRCA2 genes mutations in breast cancer development. Medical journal of the Islamic Republic of Iran. 2016; 30:369.
10. Jiang M, Jia K, Wang L, Li W, Chen B, Liu Y, Wang H, Zhao S, He Y, Zhou C. Alterations of DNA damage repair in cancer: from mechanisms to applications. Annals of Translational Medicine. 2020;8(24).
11. Pilié PG, Tang C, Mills GB, Yap TA. State-of-the-art strategies for targeting the DNA damage response in cancer. Nature reviews Clinical oncology. 2019;16(2):81-104.
12. Dias MP, Moser SC, Ganesan S, Jonkers J. Understanding and overcoming resistance to PARP inhibitors in cancer therapy. Nature reviews Clinical oncology. 2021;18(12):773-91.

13. Nelson HD, Pappas M, Zakher B, Mitchell JP, Okinaka-Hu L, Fu R. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: a systematic review to update the US Preventive Services Task Force recommendation. Annals of internal medicine. 2014;160(4):255-66.
14. Owens DK, Davidson KW, Krist AH, Barry MJ, Cabana M, Caughey AB, Doubeni CA, Epling JW, Kubik M, Landefeld CS, Mangione CM. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer: US Preventive Services Task Force recommendation statement. Jama. 2019;322(7):652-65.
15. Siu AL, US Preventive Services Task Force. Screening for breast cancer: US Preventive Services Task Force recommendation statement. Annals of internal medicine. 2016;164(4):279-96.
16. Dilmac S, Ozpolat B. Mechanisms of PARP-Inhibitor-Resistance in BRCA-Mutated Breast Cancer and New Therapeutic Approaches. Cancers. 2023;15(14):3642.
17. Welsh JL, Hoskin TL, Day CN, Thomas AS, Cogswell JA, Couch FJ, Boughey JC. Clinical decision-making in patients with variant of uncertain significance in BRCA1 or BRCA2 genes. Annals of surgical oncology. 2017; 24:3067-72.
18. Kriege M, Jager A, Hooning MJ, Huijskens E, Blom J, van Deurzen CH, Bontenbal M, Collee JM, Menke-Pluijmers MB, Martens JW, Seynaeve C. The efficacy of taxane chemotherapy for metastatic breast cancer in BRCA1 and BRCA2 mutation carriers. Cancer. 2012;118(4):899-907.
19. Bernstein-Molho R, Kaufman B, David MA, Sklair-Levy M, Feldman DM, Zippel D, Laitman Y, Friedman E. Breast cancer surveillance for BRCA1/2 mutation carriers–is "early detection" early enough? The Breast. 2020; 49:81-6.
20. Henry NL, Shah PD, Haider I, Freer PE, Jagsi R, Sabel MS. Cancer of the breast. InAbeloff's Clinical Oncology 2020: 1560-1603. Elsevier.
21. Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast cancer—epidemiology, risk factors, classification, prognostic markers, and current treatment strategies—an updated review. Cancers. 2021;13(17):4287.
22. Baretta Z, Mocellin S, Goldin E, Olopade OI, Huo D. Effect of BRCA germline mutations on breast cancer prognosis: A systematic review and meta-analysis. Medicine. 2016;95(40).
23. Zhong Q, Peng HL, Zhao X, Zhang L, Hwang WT. Effects of BRCA1-and BRCA2-related mutations on ovarian and breast cancer survival: a meta-analysis. Clinical Cancer Research. 2015;21(1):211-20.
24. van den Broek AJ, Schmidt MK, van 't Veer LJ, Tollenaar RA, van Leeuwen FE. Worse breast cancer prognosis of BRCA1/BRCA2 mutation carriers: what's the evidence? A systematic review with meta-analysis. PloS one. 2015;10(3): e0120189.
25. Afghahi A, Telli ML, Kurian AW. Genetics of triple-negative breast cancer: Implications for patient care. Current problems in cancer. 2016;40(2-4):130-40.
26. Ezenwajiaku N, Ma CX, Ademuyiwa FO. Updates on Molecular Classification of Triple Negative Breast Cancer. Current Breast Cancer Reports. 2018; 10:289-95.
27. Krüger K, Wik E, Knutsvik G, Nalwoga H, Klingen TA, Arnes JB, Chen Y, Mannelqvist M, Dimitrakopoulou K, Stefansson IM, Birkeland E. Expression of Nestin associates with

BRCA1 mutations, a basal-like phenotype and aggressive breast cancer. Scientific reports. 2017;7(1):1089.
28. McAlpine JN, Porter H, Köbel M, Nelson BH, Prentice LM, Kalloger SE, Senz J, Milne K, Ding J, Shah SP, Huntsman DG. BRCA1 and BRCA2 mutations correlate with TP53 abnormalities and presence of immune cell infiltrates in ovarian high-grade serous carcinoma. Modern Pathology. 2012;25(5):740-50.
29. Mylavarapu S, Das A, Roy M. Role of BRCA mutations in the modulation of response to platinum therapy. Frontiers in oncology. 2018; 8:16.
30. Copson ER, Maishman TC, Tapper WJ, Cutress RI, Greville-Heygate S, Altman DG, Eccles B, Gerty S, Durcan LT, Jones L, Evans DG. Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. The lancet oncology. 2018;19(2):169-80.
31. Peyraud F, Italiano A. Combined PARP inhibition and immune checkpoint therapy in solid tumors. Cancers. 2020;12(6):1502.
32. McCann KE. Advances in the use of PARP inhibitors for BRCA1/2-associated breast cancer: talazoparib. Future Oncology. 2019;15(15):1707-15.
33. Garrido-Castro AC, Lin NU, Polyak K. Insights into molecular classifications of triple-negative breast cancer: improving patient selection for treatment. Cancer discovery. 2019;9(2):176-98.
34. Piccinin C, Panchal S, Watkins N, Kim RH. An update on genetic risk assessment and prevention: the role of genetic testing panels in breast cancer. Expert Review of Anticancer Therapy. 2019;19(9):787-801.
35. Burke W, Parens E, Chung WK, Berger SM, Appelbaum PS. The challenge of genetic variants of uncertain clinical significance: a narrative review. Annals of Internal Medicine. 2022;175(7):994-1000.
36. Shkedi-Rafid S, Gabai-Kapara E, Grinshpun-Cohen J, Levy-Lahad E. BRCA genetic testing of individuals from families with low prevalence of cancer: experiences of carriers and implications for population screening. Genetics in medicine. 2012;14(7):688-94.
37. Morganti S, Tarantino P, Ferraro E, D'Amico P, Viale G, Trapani D, Duso BA, Curigliano G. Complexity of genome sequencing and reporting: Next generation sequencing (NGS) technologies and implementation of precision medicine in real life. Critical reviews in oncology/hematology. 2019; 133:171-82.
38. Walter W, Pfarr N, Meggendorfer M, Jost P, Haferlach T, Weichert W. Next-generation diagnostics for precision oncology: Preanalytical considerations, technical challenges, and available technologies. InSeminars in Cancer Biology 2022; 84: 3-15). Academic Press.
39. Obeagu EI, Obeagu GU. Breast cancer: A review of risk factors and diagnosis. Medicine. 2024 Jan 19;103(3):e36905.
40. Obeagu EI, Babar Q, Vincent CC, Udenze CL, Eze R, Okafor CJ, Ifionu BI, Amaeze AA, Amaeze FN. Therapeutic targets in breast cancer signaling: A review. Journal of Pharmaceutical Research International. 2021 Dec 13;33(56A):82-99.
41. Mohamed QH, Obeagu EI. Genetic Heterogeneity in Breast Cancer: Implications. Elite Journal of Health Science. 2024;2(1):20-24.
42. Mohamed AF, Obeagu EI. Genetic Influence on Breast Cancer Progression: A Molecular Perspective. Elite Journal of Medica Science. 2024;2(1):19-22.

43. Obeagu EI, Muhimbura E, Kagenderezo BP, Nakyeyune S, Obeagu GU. An Insight of Interleukin-6 and Fibrinogen: In Regulating the Immune System. J Biomed Sci. 2022;11(10):83.
44. Obeagu EI, Babar Q, Vincent CC, Anyanwu CO, Uduchi IO. Advances in Therapeutic Strategies of Immunotherapy in Cancer Treatment. World Journal of Pharmacy and Pharmaceutical Sciences. 2021 Jun 18;10(8):2144-64.
45. Aizaz M, Khan M, Khan FI, Munir A, Ahmad S, Obeagu EI. Burden of Breast Cancer: Developing Countries Perspective. International Journal of Innovative and Applied Research. 2023;11(1):31-7.