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TALAZOPARIB: A GAME-CHANGER IN TARGETED BREAST CANCER THERAPY-INNOVATIVE, IMPACT AND INVESTMENT

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ABSTRACT

Background: Breast cancer continues to be the most common malignancy in women all over the world. The defects in homologous recombination DNA repair by germline BRCA1/2 mutations leave the organism vulnerable to poly(ADP-ribose) polymerase (PARP) inhibition. Talazoparib is a strong PARP inhibitor that is used as a treatment for advanced breast cancer with no HER2 and with BRCA mutations. **Methods:** The data on clinical efficacy, safety and cost-effectiveness were assessed based on evidence of key clinical trials (ABRAZO, EMBRACA) and pharmacoeconomic studies. **Results:** Talazoparib was significantly better in terms of progression-free survival, objective response rates and health-related quality of life as compared to conventional chemotherapy. The EMBRACA trial reported a median progression-free survival of 8.6 months as compared to chemotherapy of 5.6 months. Treatment was mostly well tolerated and anaemia was the most reported adverse event. Nevertheless, economic analysis shows that at the present prices, it is not very cost-effective. **Conclusion:** Talazoparib is one of the significant steps forward in the tailored treatment of breast cancer with BRCA mutations. Genetic testing should be made more affordable and accessible to increase its clinical and global benefits.

KEYWORDS

Talazoparib, Breast cancer, Anemia and Chemotherapy.

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INTRODUCTION

Background Information

Breast cancer stands as the leading malignancy in women who manifest hormone receptors that test positive for ER, PR and HER2 and will present symptoms including lumps which often cause pain. BRCA mutations combined with age, obesity and lifestyle factors promote cancer development although inadequate screening presents a significant

issue for developing countries (Beata Smolarz *et al*, 2022)[1].

Global breast cancer diagnosis numbers reached 2.3 million in 2020 while 685,000 people died from the disease with industrialized countries experiencing higher detection rates but developing regions experienced higher mortality rates because of delayed medical treatment (Melina Arnold *et al*, 2022)[2].

Drug and mechanism of action

Talazoparib, a PARP inhibitor, is approved for locally advanced or metastatic HER2-negative breast cancer in patients with BRCA1 or BRCA2 mutations (Laura Cortesi *et al*, 2021)[4].

Clinical trial

In the ABRAZO Phase II trial Talazoparib demonstrated a CBR range of 38-66% together with PFS extending up to 4.0-5.6 months in BRCA-mutated breast cancer.

The EMBRACA Phase III trial demonstrated Talazoparib extended PFS to 8.6 months compared to 5.6 months together with improving ORR to 62.6% and enhancing QOL in advanced breast cancer patients with BRCA mutations and without HER2 positivity.

The tolerability profile of Talazoparib surpassed chemotherapy as a treatment strategy because anemia affected 39.2% of patients while neutropenia and thrombocytopenia developed in some individuals but this led to minimal treatment discontinuations.

Patients with BRCA-mutated, HER2-negative breast cancer experienced an 8.6-month improvement in PFS along with higher ORR (62.6% vs. 27.2%) and better QOL while also showing promising results in HR+ and TNBC groups but an OS benefit needs confirmation (Sheridan M. Hoy, 2018)[5].

Cost-effectiveness

Talazoparib improves survival and increases Quality-Adjusted Life Years (QALYs) for BRCA-mutated breast cancer patients.

A Spanish analysis found that Talazoparib is not cost-effective compared to chemotherapy at willing to pay (WTP) levels of €21,000 to €60,000 per QALY, requiring an 85% price reduction.

However, genetic testing can improve QALY outcomes by guiding treatment selection.

Talazoparib therapy offers improved progression-free survival (PFS) and overall survival (OS), increasing QALYs despite higher costs and it enhances health-related quality of life compared to chemotherapy.

The QALY benefits of Talazoparib can be enhanced by reducing prices or changing insurance coverage limits, along with combination strategies and targeted treatments (Haiying Ding, *et al*, 2022)[6].

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Talazoparib's PFS data outperformed standard chemotherapy and led to better PFS outcomes than conventional chemotherapy.

Further, the initial OS findings were positive but require furthermore research ahead.

Offers lasting benefits for patients with hormone receptor-positive or triple-negative breast cancer.

Common side effects were anemia, neutropenia, nausea and fatigue, managed by dose adjustments (Jennifer K. Litton, *et al*, 2018)[7].

LIMITATIONS

The most frequently reported adverse effect of Talazoparib involves anemia at a rate of 39.2%. In contrast, neutropenia and thrombocytopenia also occur but need dose adjustments before patients can continue receiving therapy because the drug is better tolerated than conventional chemotherapy (Sheridan M. Hoy, 2018)[5].

The existing pricing of Talazoparib will not be cost-effective until manufacturers decrease rates by 85% due to reimbursement restrictions throughout different regions (Haiying Ding, *et al*, 2022)[6].

The research shows that Talazoparib extends PFS and ORR, but researchers have not established clear OS advantages, especially regarding patients who do not carry BRCA mutations (Haiying Ding, *et al*, 2022)[6].

The availability of gene testing programs remains limited and expensive drug costs result in reduced patient access and treatment benefits for developing countries due to poor infrastructure in resource-limited regions (Haiying Ding, *et al*, 2022)[6].

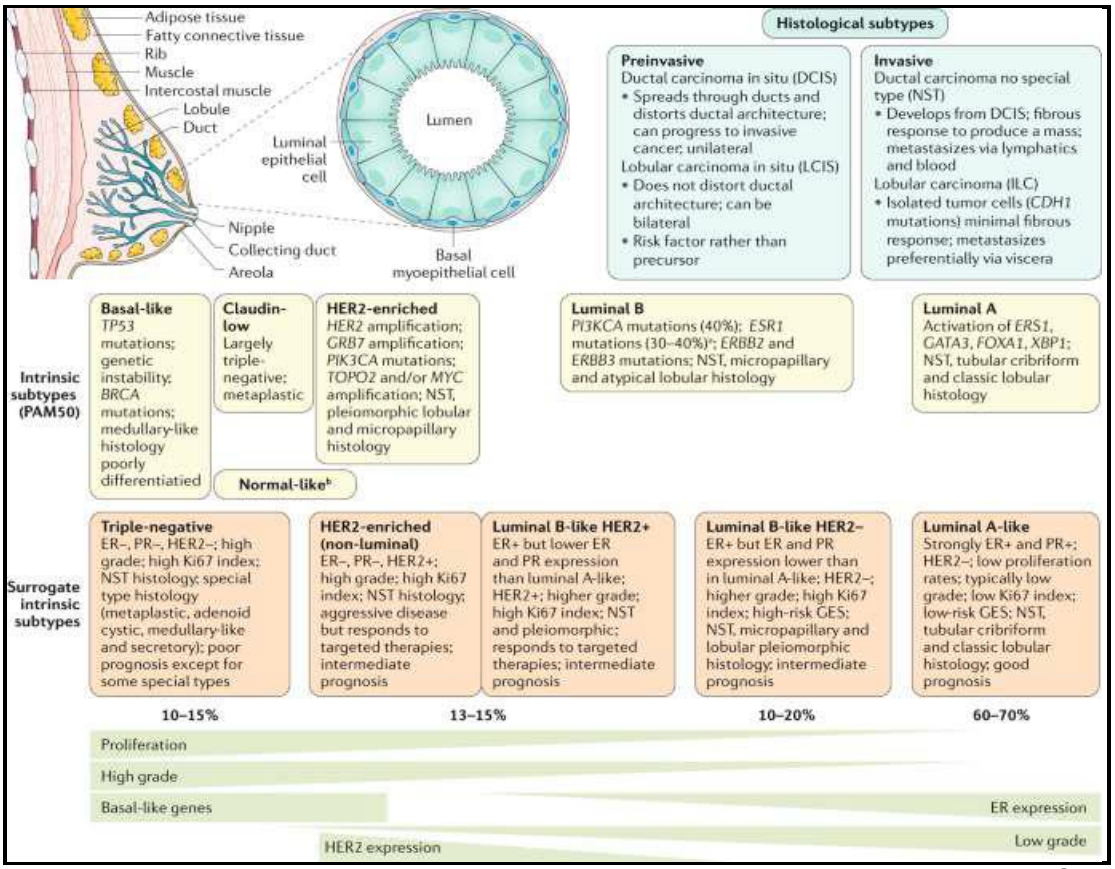

Figure No.1: Pathophysiology of breast cancer (Nadia Harbeck *et al*, 2019)[3]

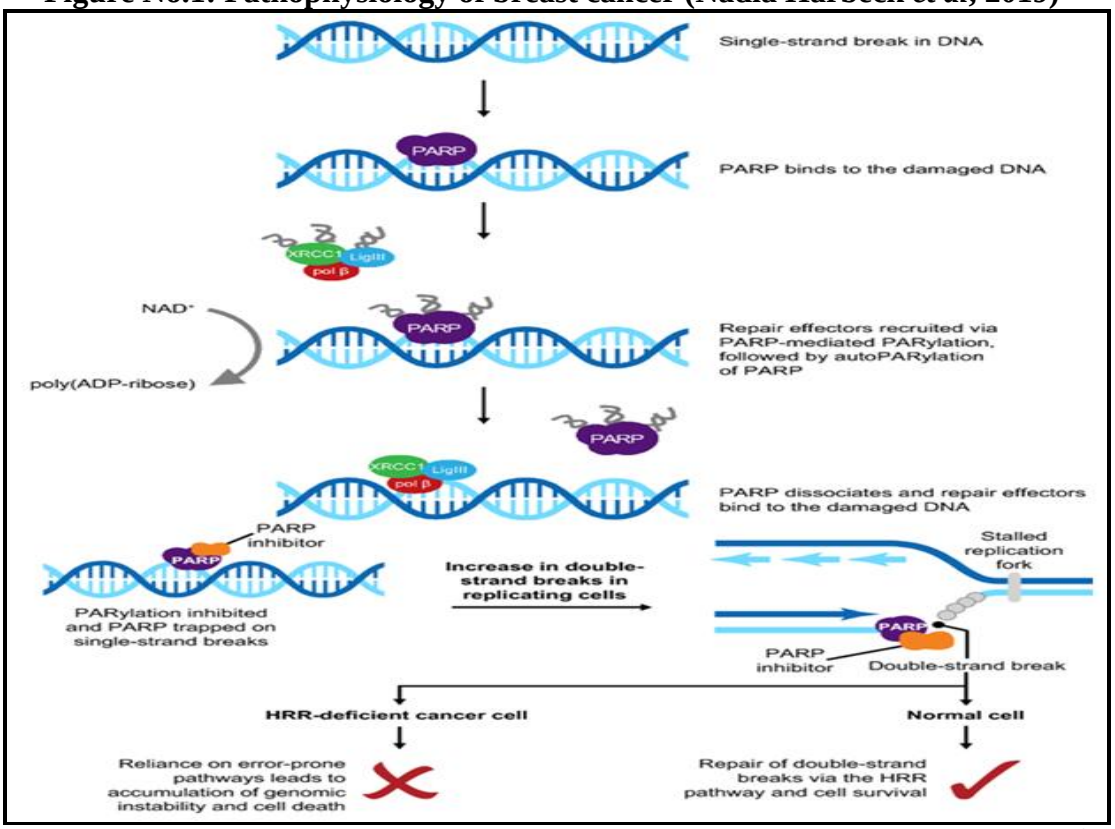

Figure No.2: Mechanism of Action of Talazoparib (Laura Cortesi *et al*, 2021)[4]

DRUG DEVELOPMENT

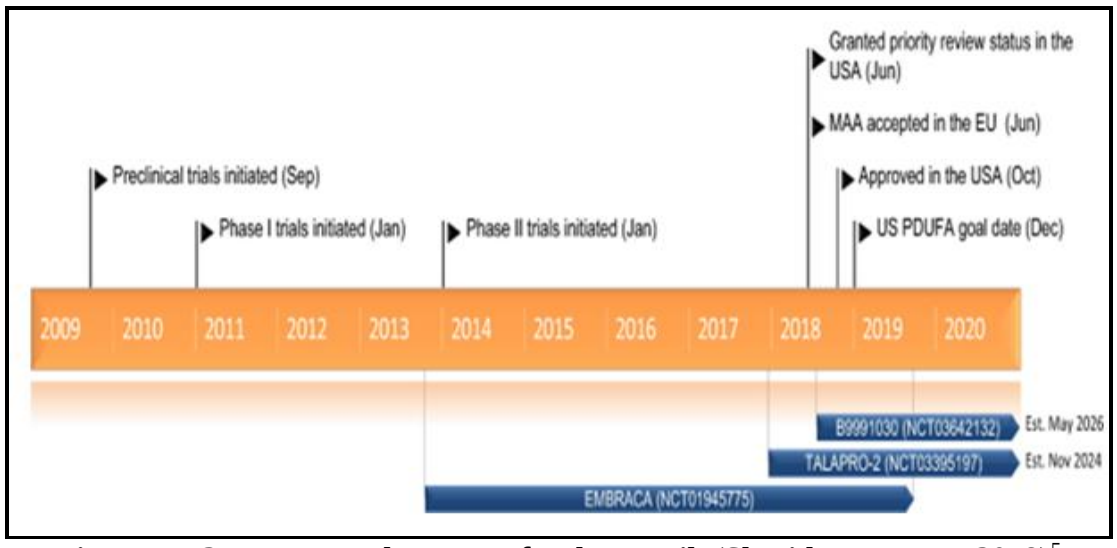

Figure No.3: Drug Development of Talazoparib (Sheridan M. Hoy, 2018)[5]

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CONCLUSION

Similar to chemotherapy, the tolerability of TP-1066 shows improved results, yet patients must adapt their dose due to side effects of anemia (39.2%), neutropenia, and thrombocytopenia (Sheridan M. Hoy, 2018)[5].

Talazoparib shows promise for BRCA1/2-mutated HER2-negative advanced breast cancer, but an 85% price reduction is needed for better patient access (Haiying Ding, *et al*, 2022)[6].

The potential combination of Talazoparib with PD-L1 inhibitors to treat HR+ and TNBC (Jennifer K. Litton, *et al*, 2018)[7].

The accessibility to genetic testing programs remains limited while drug prices remain high which especially affects developing nations (Haiying Ding, *et al*, 2022)[6].

Studies in real-world settings are necessary to prove the effectiveness of disease control period improvement, quality-adjusted life year increases and cost-effectiveness (Jennifer K. Litton, *et al*, 2018)[7].

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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