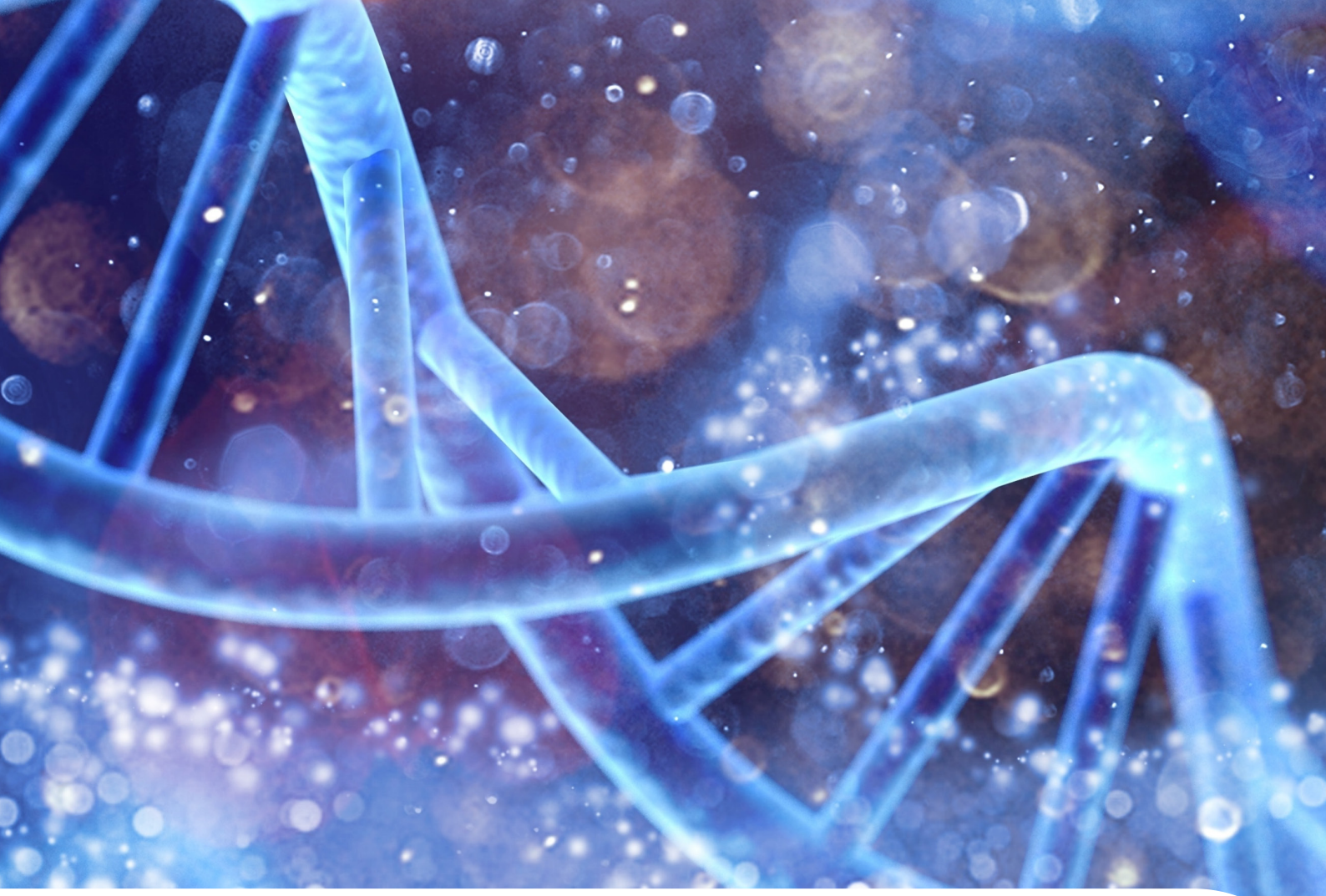

The use of *PARP Inhibitors* as Chemoprevention: A vision for the future

Joint position statement
September 2025

BREAST CANCER NOW The research & support charity
CANCER RESEARCH UK
OVARIAN CANCER ACTION
Pancreatic CANCER UK
PROSTATE CANCER UK
worldwide cancer research
Yorkshire Cancer Research

Background

This Position Statement represents an expression of interest from a collaboration of seven charities, to explore the viability of whether poly (ADP-ribose) polymerase (PARP) inhibitors can be used as a chemo preventative treatment for people at high risk of hereditary cancers as part of a drive toward a future of precision cancer prevention. This includes primary prevention of cancer but could also include preventing the recurrence of cancer or preventing progression of low-risk cancers in BRCA carriers.

The Position Statement focuses on BRCA1 and BRCA2 mutations (BRCAm) for two primary reasons. Firstly, they are two of the most commonly mutated genes that increase the risk of hereditary cancers and secondly, PARP inhibitors are currently licensed for treating BRCA-related cancers. However, it is important to note there are other genes, those that encode DNA repair proteins, that are relevant to the anti-cancer mechanism of action of PARP inhibitors. In the future, as increasing levels of genetic testing identifies more people who have one or more hereditary genetic mutations putting them at higher risk of cancer, and as more genes of interest are discovered, the scope for use of PARP inhibitors in cancer treatment and prevention is likely to expand.

People with BRCAm have a significantly higher lifetime risk for developing some types of cancer, including breast, ovarian, prostate and pancreatic cancers among others. Currently, there are a number of ways in which people may be able to access genetic testing, including: having a family history that means an individual is considered significantly high enough risk, once a family member is diagnosed with cancer via cascade testing; or through other family links such as being part of the Ashkenazi Jewish community (testing programme active to Autumn 2025). Furthermore, new genetic screening research studies are looking to establish the acceptability and efficacy of screening the general population for high-risk cancer genes, which if successful could lead to the identification of more people with BRCAm as well as mutations in other DNA repair genes.

People identified as being BRCAm carriers currently have a number of preventative options for reducing their risk of cancer in the future, such as preventative surgery, enhanced screening and chemoprevention medications like tamoxifen; however, these may not be suitable for all BRCA carriers. Risk reduction surgery may not always be an option however, particularly for men, and where it is an option, the surgery can be extensive and life-altering, for example removing the option for women to have children in the future.

Currently, it is estimated that around 1 in 400 people[1] in the UK general population are BRCA mutation carriers, but it is thought that a high proportion of people with a high-risk gene for cancer are unaware of this. The prevalence of BRCAm is significantly higher in certain populations – such as those of Ashkenazi Jewish descent in whom around 1 in 40 people[2] have the mutation - due to specific founder effects. This means, there could be over 170,000 adults who have a BRCA mutation across the UK, the majority of whom will be unaware they are at increased risk of cancer.

In 2014, Lynparza, also known as Olaparib, became the first PARP inhibitor drug to be approved for the treatment of people with hereditary BRCA-related ovarian cancer. Since 2014, a number of additional licences have been granted for the use of PARP-inhibitors to treat BRCA-related cancer, and in addition further PARP inhibitors have been developed such as Niraparib, Rucaparib and Talazoparib.

[1] NHS England, National Genomics Education Programme. *BRCA1 and BRCA2.* 2023. Accessed: 13/06/2025. Available from: https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/brca1-and-brca2/#prevalence

[2] Sarig K, Oxley S, Kalra A, Sobocan M, Fierheller CT, Sideris M, et al. *BRCA awareness and testing experience in the UK Jewish population: a qualitative study.* J Med Genet. 2024;61(7):716-25.

A vision for *the future*

Findings from the OlympiA trial[3] indicate there maybe an effect of PARP inhibitors in the prevention of a second primary cancer when they are used as a treatment for breast cancer in people with a BRCA mutation.

Acting as thought leaders in this space, this collaboration of seven charities is keen to explore whether PARP inhibitors could, in the future, be used as a preventative treatment for people with a BRCA mutation as an example of precision cancer prevention.

Next steps

Prior to any clinical trials to test PARP inhibitors as a method of cancer prevention there are several critical pieces of information required. Patient preference studies must be undertaken to establish whether chemoprevention with PARP inhibitors would be an acceptable option for people considering other risk reducing options, such as surgery. Pre-clinical work is also a prerequisite to provide additional evidence and understanding of the preventative effects of PARP inhibitors and to establish a safe and effective dose as well as an appropriate dosing schedule.

'Window of opportunity' trials, where BRCAm carriers receive PARP inhibitors before risk reducing surgery, present an interesting scenario to start developing an understanding of how PARP inhibitors may be used in a preventative context. This could include testing of biomarkers predictive of response and exploring the impact of different dosing regimen.

Working *together*

Prevention research is notoriously challenging to do, due in part to long follow up that is often required and significant engagement from participants taking part. According to the International Cancer Research Partnership, of all projects active in 2023, there were 1,703 cancer research projects lead by UK Principal Investigators, of these 93 were classified as prevention research, however, not all of these were focused on primary prevention.[4] In terms of prevention research funding, the NIHR data of active awards indicates a cancer prevention portfolio value of £22.0m compared to an overall active cancer portfolio value of £195.4m.[5] These figures cause pause for thought when considered within the current national policy context, which has a renewed focus on shifting healthcare from sickness to prevention and prioritises realising the UK's potential as a global leader in life sciences. Therefore, research into use of PARP inhibitors as an example of precision prevention, perhaps leading to a chemoprevention trial in the future could bring significant patient benefit in an understudied field, and in a space where we must acknowledge a growing need over the next decade and beyond as more people with BRCAm are identified.

The charities part of this collaboration are committed to exploring how precision cancer prevention can be driven forward and are supportive of endeavours in this field of research. While some of the charities in the collaboration are able to contribute funding towards work in this space (either dedicated or via open competition), others are able to support this research by sharing with their networks, providing access to people with BRCAm.

[3] Geyer CE, Jr., Garber JE, Gelber RD, Yothers G, Taboada M, Ross L, et al. *Overall survival in the OlympiA phase III trial of adjuvant olaparib in patients with germline pathogenic variants in BRCA1/2 and high-risk, early breast cancer.* Annals of Oncology. 2022;33(12):1250-68.

[4] International Cancer Research Partnership. *Search ICRP Database (filtered by 2024, UK PI and Total Projects vs CSO 3 (Prevention)).* 2023. Accessed: 25/03/2025. Available from: https://www.icrpartnership.org/db_search?sid=65139

[5] National Institute for Health and Care Research. *Advanced Search Form.* 2025. Accessed: 25/03/2025. Available from: https://fundingawards.nihr.ac.uk/advanced-search

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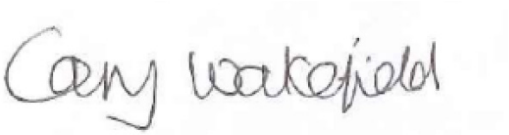

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