BRCA in DNA damage repair, cancer development and targeted therapy

BRCA mutation is a key driver of breast cancer development[1,2]

Different types of DNA damage are repaired via distinct DNA repair pathways

BRCA1 and BRCA2 are critical components of homologous recombination repair (HRR)

BRCA

Pathogenic BRCA mutation results in dysfunctional HRR which may lead to the development of cancer if accumulating DNA damage can not be repaired

BRCA mutation represents an opportunity for targeted therapy[1]

- **In normal cells** the HRR pathway is functional when there is at least one functional copy of each BRCA gene
- **In BRCA-mutated tumor cells** the HRR pathway is not functional due to homozygous mutation in one or both BRCA genes

- **Cancer-specific synthetic lethality** can be induced by inhibiting functional DNA repair pathways in tumor cells where one or more repair pathways are already lost

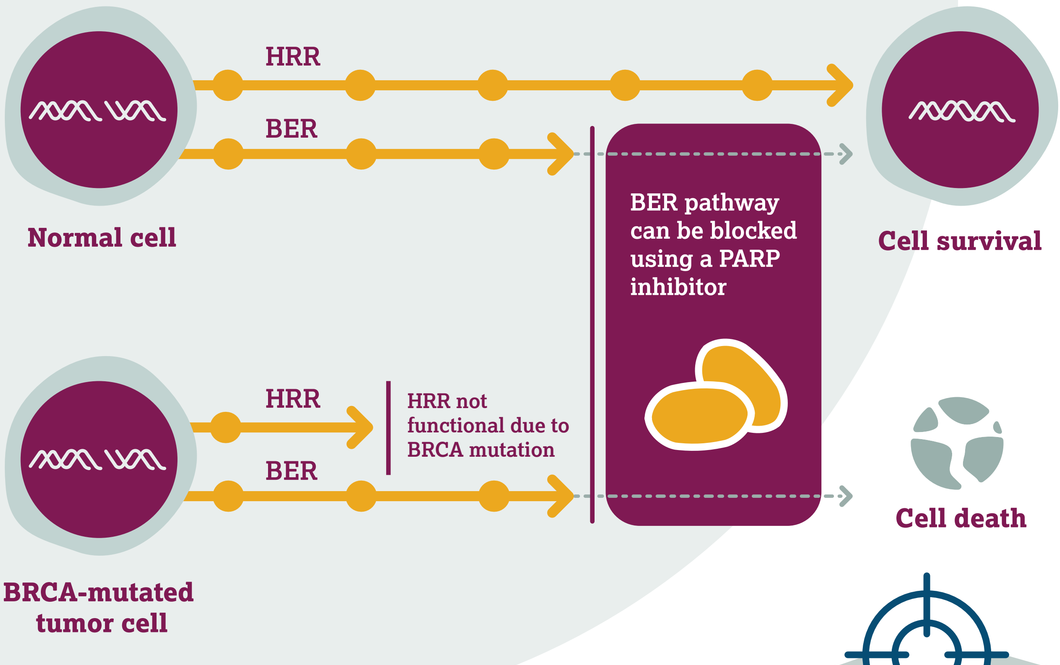

Figure developed by AZ based on data from ref 1 and 2

BER, base excision repair;
HRR, homologous recombination repair

Test early for BRCA mutations

1.O'Connor MJ. Mol Cell. 2015;60(4):547-560; 2.Lord CJ & Ashworth A. Nature. 2012;481:287-294.

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