PARP Inhibitor

In healthy cells, DNA damage occurs and is repaired by proteins, such as poly ADP-ribose polymerase (PARP), so the cell can continue to function. This damage can be spontaneous or the result of environmental factors like radiation or some chemicals.

Cancer cells also experience damage to their DNA, just like healthy cells, and use proteins such as PARP to repair the damaged DNA.

**Mechanism of Action**

- **Single Strand Break (SSB)**
  - PARP recruited; PARylation initiation
  - Ribosylation
  - PARP inhibition
  - Accumulation of DNA damage
  - Cell Death

- **SSB converts to Double Strand Break (DSB)**
  - PARP inhibition
  - Replication fork collapses
  - PARP1
  - HRD tumors (may be BRCAmut or BRCAwt)
  - Accumulation of DNA damage
  - Cell Death

- **Platinum causes DSB**
  - PARP inhibition
  - Replication forks collapse at additional sites of damage
  - PARP inhibition causes more DSBs
  - Accumulation of DNA damage
  - Cell Death

PARP inhibitors block the PARP protein. That means the damaged DNA can’t be repaired in the cancer cell, so the DNA accumulates more and more damage, turning from single-strand breaks to double strand breaks. This accumulation can lead to the death of the cancer cell.

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**References**


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**Abbreviations**

- DSB: Double strand break
- HRD: Homologous recombination deficiency
- PARP: Poly ADP-ribose polymerase
- PR: Partial response
- SSB: Single strand break