PARP INHIBITION IS A THERAPEUTIC STRATEGY IN OVARIAN CANCER

DNA repair involves a complex protein network

**TYPE OF DAMAGE**
- Single-Strand Breaks
- Double-Strand Breaks
- Bulky Adducts
- Base Mismatches, Insertions, Deletions

**REPAIR PATHWAY**
- Base Excision Repair
- Homologous Recombination
- Nucleotide Excision Repair
- Mismatch Repair

**KEY REPAIR ENZYMES**
- PARP-1, XRCC1, DNA ligase III
- BRCA1/2, ATM, RAD51
- ERCC4, ERCC1
- MSH2, MLH1

**PROPOSED PARP INHIBITOR MECHANISM OF ACTION**
- PARP inhibitors prevent repair of single-strand breaks
- Accumulation of single-strand breaks leads to double-strand breaks
- Cells deficient in homologous recombination cannot repair double-strand breaks, triggering cell death
- BRCA1/2 is among the most frequently mutated DNA repair genes in ovarian cancer

PARP inhibition is synthetically lethal for tumors with homologous recombination deficiencies

Several PARP inhibitors are currently approved for patients with ovarian cancer

Hematologic adverse events are commonly associated with use of PARP inhibitors

Ongoing clinical trials are evaluating PARP inhibition across lines of therapy and in combination regimens

For additional content on this topic, please visit www.OvarianCancerSpotlight.com

BRCA, breast cancer susceptibility gene; PARP, poly ADP ribose polymerase