Report from Stand Up 2 Cancer Scientific Summit
PARP inhibitors: Beyond BRCA1 and BRCA2

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I spent three days at the Stand Up 2 Cancer Scientific Summit January 23 - 25 where I have proudly served on the Scientific Advisory Committee since its inception in 2008. The summit brings together some of the top oncologists and researchers from around the world to discuss their latest findings on many types of cancer. It is truly one of my favorite conferences of the year because it is small enough to be an intimate conference with time for discussion and because the collaborative philosophy that has been infused by the founders makes for very significant cross functional learnings.

The ovarian cancer dream team presented their progress report as a part of the conference. I will not review progress on each of their specific aims but will instead focus on one that has much interest for women "in the fight" against ovarian cancer, namely their aim of looking at mutations that confer sensitivity to PARP inhibitors. What many people know is that mutations in the BRCA1 and BRCA2 genes confer sensitivity to PARP inhibitors and that two drugs are currently FDA approved for ovarian cancer: Lynparza (olaparib) and Rubraca (rucaparib) and three additional drugs are in clinical trials: niraparib, veliparib and talazoparib. Interestingly, the prostate cancer dream team presented case studies of men with metastatic prostate cancer with BRCA2 mutations that had responses to olaparib. This has previously been reported at an AACR meeting.

For a number of years, people have been studying factors that are associated with inherited risk of cancer. BRCA1 and 2 are proteins found in the DNA damage repair pathway* and it is well established that germline (inherited) mutations in BRCA1 and BRCA2 account for 5 - 10% of breast cancers and 10 - 18% of ovarian cancers. What is now understood is that other proteins involved in the DNA repair pathway also contribute to the inherited risk for another 6% of ovarian cases including genes called ATM, RAD51, BRIP1, PALB2 to name a few (for review, click here). Importantly, there are now updated recommendations from the National Comprehensive Cancer Network (NCCN) which include genetic screening for alterations in these genes.

In the laboratory, scientists have been studying whether alterations in these other genes in the DNA repair pathway confer sensitivity to PARP inhibitors similar to that observed with BRCA mutations. Now these concepts are being tested in the clinic and at the SU2C scientific summit, Dr. Swisher and her ovarian cancer dream team provided an update of their findings. As we gain a better understanding of which gene alterations impart sensitivity to PARP inhibitors, new treatment options will be revealed. At Clearity, we have advocated for tumor molecular profiling since our inception. The testing that we help facilitate includes analysis of these and other genes in the DNA repair pathway. Knowing this information can help determine the appropriateness of a PARP inhibitor clinical trial - even for those women who have normal BRCA1 and BRCA2 genes.

**There are different types of DNA repair pathways. To keep it simple, I am using this general term but for the scientists reading the article, you will recognize that I am referring to homologous recombination repair of double-strand DNA breaks.*