

HRD-positive breast cancer patients fare better with adjuvant AC chemotherapy

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People with tough-to-treat triple negative breast cancer, whose tumors also don't allow for double-strand DNA repair, fare better when treated with a common adjuvant breast cancer chemotherapy combination, according to results from a SWOG clinical trial.

Published in *Annals of Oncology*, the trial results show that a well-established drug combination - adjuvant doxorubicin and cyclophosphamide (AC) chemotherapy - works well in this patient population. The results also show the value of collecting and preserving [cancer](#) tumor tissue. Priyanka Sharma, MD, of University of Kansas Cancer Center, and her team used nearly 20-year-old tumor samples stored in SWOG's biospecimen bank to conduct their analysis.

"Banking tissue in cancer research is a smart investment," Sharma said. "Tissue collected for one research study can be used for others, creating value for [patients](#), investigators, and for the public who funds our SWOG research."

Sharma is an associate professor of medicine and a breast cancer oncologist at University of Kansas Cancer Center, and the vice chair of the breast committee for SWOG, the cancer clinical [trials](#) group that is part of the National Cancer Institute's (NCI) publicly funded National Clinical Trials Network (NCTN). Sharma has spent over a decade conducting research to better understand triple negative breast cancer. It's a catch-all term for cancers that test negative for three common factors that fuel breast cancer growth: estrogen receptors, progesterone

receptors, and the HER2 gene. Triple negative breast cancers tend to grow faster and spread more frequently, and many current therapies aren't effective in slowing or stopping their growth.

How can physicians better treat people diagnosed with triple negative breast cancer? This question drove Sharma and her team to launch their SWOG study. Emerging evidence shows that many breast cancer patients' tumors have what is known as homologous recombination deficiency (HRD). This means that their cells have trouble repairing double-strand DNA breaks - a deficiency that can contribute to cancer. To better understand the link between HRD and triple negative breast cancer, and to test a hunch that repair-inhibiting therapies like AC chemotherapy would be effective in treating it, Sharma wrote a proposal focused on HRD, which was approved by SWOG and NCI. This allowed Sharma's team to access the SWOG biospecimen bank and use tissue from S9313 trial.

The SWOG bank is a treasure trove for researchers, holding more than 800,000 tissue, blood, and other biological samples taken to conduct SWOG trials. Sharma and her team used tissue gathered for S9313, a trial assessing the effectiveness of AC chemotherapy in patients with high- and moderate-risk breast cancers. The S9313 study stopped enrolling patients in 1997, but tissue samples from those patients remained, preserved in blocks of paraffin wax.

Investigators isolated genomic DNA and RNA from 425 of these samples, and could determine HRD status in 379 of them - an 89 percent success rate. Of those 379 cases, the team found that 67 percent had positive HRD status. After reviewing treatment responses to AC chemotherapy recorded in the S9313 trial, the team found that positive HRD status was associated with better disease-free survival. Put another way, patients whose tumor could not efficiently repair DNA damage (induced by AC chemotherapy) were more likely to remain cancer-free

10 years after AC chemotherapy treatment.

"We learned three interesting things from this trial," Sharma said. "First, we showed that assays tested in our study worked well in very old tissue samples. We also learned that 25 percent of triple negative breast cancer patients harbored BRCA 1 or BRCA2 mutations and tumors in these patients were HRD positive. However, presence of HRD was not restricted to just patients with BRCA mutations, as among patients without BRCA mutations, 55 percent also demonstrated tumor HRD. Finally, and most importantly, we learned that 67 percent of triple negative [breast cancer patients](#) - a solid majority - respond well to a standard, backbone chemotherapy combination. So, while, AC chemo is an old treatment, for many, it's still a good one. HRD status is a biomarker that, when identified, can potentially help a physician best tailor a [chemotherapy](#) treatment for that particular triple negative [breast cancer patient](#)."

More information: P Sharma et al, Impact of homologous recombination deficiency biomarkers on outcomes in patients with triple-negative breast cancer treated with adjuvant doxorubicin and cyclophosphamide (SWOG S9313), *Annals of Oncology* (2017). [DOI: 10.1093/annonc/mdx821](#)

Provided by SWOG

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