Deep sequencing of breast cancer tumors to predict clinical outcomes after single dose of therapy

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New research from University Hospitals (UH) Case Medical Center Seidman Cancer Center and Case Comprehensive Cancer Center at Case Western Reserve University examined how changes in the genetic composition of breast cancer tumors after brief exposure to either biologic therapy or chemotherapy can predict future clinical outcomes in patients.

Results showed that through deep genome sequencing, a reduction in the most commonly mutated genes in breast cancer could be observed after just one dose of preoperative therapy. Deep sequencing is a process that involves sequencing the same region multiple times to identify mutations within tumors that have an importance in cancer evolution. These new findings were presented during the 2013 San Antonio Breast Cancer Symposium.

"Genomics is the new frontier of cancer research, and this study shows that we may be able to accurately determine what treatment methods will and will not be effective for individual patients after just one dose of medicine," said Lyndsay Harris, MD, study investigator and Director, Breast Cancer Program, UH Seidman Cancer Center and Professor of Medicine at Case Western Reserve University School of Medicine. "The ability to understand potential clinical outcomes for patients earlier in the treatment process would provide physicians with better opportunity to personalize patients' medicines according to their own tumor

responses."

More than 209,000 patients in the U.S. are diagnosed with breast cancer each year. The anticipated outcome of studying the genetic makeup of breast cancer patients is to determine who will benefit most from certain drug therapies and to use that information to create a personalized treatment plan for each patient involved. Dr. Harris and team are currently integrating whole genome profiles with deep sequencing data as they spearhead a new study at UH Seidman Cancer Center to validate these initial findings presented in San Antonio.

Dr. Harris' co-presenters are: Nicole Williams, Vinay Varadan, Kristy Miskimen, Aditi Vadodkar, Debora Poruban,, Simone Edelheit, Hannah Gilmore, Steve Maximuk, Natalie Sinclair, Kimberly Lezon-Geyda, Maysa Abu-Khalaf, William Sikov, University Hospitals Case Medical Center/Case Western Reserve University, Cleveland, OH; Yale University School of Medicine; Yale Comprehensive Cancer Center, New Haven, CT; Warren Alpert Medical School of Brown, Providence, RI.

About the Studies

P1-08-16: Poster Session 1: Prognosis and Response Prediction: Response Predictive Factors

Deep sequencing of breast tumor biopsies reveals an association between pathologic complete response (pCR) and reduction of TP53 clonal abundance upon brief exposure to therapy, Wednesday 12/11, 5:00 PM -7:00 PM

Investigators evaluated 120 Stage IIA to IIIB breast cancer patients and compared a first biopsy after brief exposure to either biologic or chemotherapy treatment with a second biopsy taken after surgery.

Researchers utilized deep genomic sequencing to quantify the abundance of clonal mutations in breast core biopsies, assess changes in these mutations after brief exposure to a targeted therapy and then evaluate the corresponding change in abundance of these mutations after exposure. This process of quantifying and monitoring clonal mutations between initial therapy exposure and surgery allowed researchers to determine how changes in the abundance of these mutations related to a patient's response to preoperative therapy. Through this analysis, investigators determined that clonal abundance upon brief exposure to therapy may be associated with clinical outcomes.

Provided by University Hospitals Case Medical Center