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First large-scale study of whole-genome testing helps identify best treatment for women with advanced breast cancer

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The first large-scale study testing all the DNA—the entire genome—of tumor cells from more than 400 women with advanced breast cancer has identified individuals with a good chance of benefiting from specific treatments already being tested in clinical trials.

The findings, published in *The Lancet Oncology*, may help physicians more accurately choose treatments that will target genomic alterations (DNA copy numbers or mutations) in women with advanced breast cancer and could also guide the design of clinical trials and the development of new drugs.

"Until now genetic testing has only analysed a limited number of genes to select which targeted drugs are suitable for individual patients and many treatment opportunities may be missed", explains study leader Professor Fabrice André from the Institute Gustave Roussy in France.

"For the first time, we have shown that scanning the whole genome can identify both frequent and rare genomic alterations and can be done in clinical practice in large numbers of women, enabling us to match alterations with individually targeted drugs in patients whose metastatic disease has progressed."

The goal of the SAFIR01 trial was to see whether whole-genome analysis (comparative genomic hybridisation [CGH] array and Sanger

sequencing) could identify unique characteristics and abnormal genes in the metastatic tissue which could then be targeted for treatment in appropriate phase 1 and 2 clinical trials.

The investigators looked at the quality of tumour samples, the proportion of women for which the genomic analyses could be done, and the proportion for which a targeted therapy could be offered.

They took biopsy samples from 407 patients from 18 centres across France. Serious adverse events were reported in 9 patients (2%), and in four patients the biopsy confirmed an alternative diagnosis.

Whole-genome analysis (CGH array) was achieved in around two-thirds of patients. Around half (46%) of the 423 enrolled patients were found to have a targetable genomic alteration, and 39% a rare alteration, for many of which no treatments currently exist.

"So far 55 (13%) of those enrolled (28% of those with targetable alterations) have been matched with new treatments being tested in clinical trials. This emphasises the need to increase the range of drug trials. Our goal is to have 30% of patients in clinical trials testing therapies targeting the alterations identified in their tumours", said André.

He concludes, "Our finding indicate that large molecular screening programs, performed in the context of clinical trials, are helpful to see whether a patient with metastatic cancer could be eligible for a targeted therapy matched to a genomic alteration."

Writing in a linked Comment, Charles Swanton from the Cancer Research UK London Research Institute discusses the clinical challenges of implementing more precision treatment in breast cancer, saying that, "SAFIR01 provides a stark reminder that understanding of biological

drivers of metastatic disease progression is basic."

He concludes, "In view of the challenges highlighted by SAFIR01, efforts to accelerate genomic analyses for personalised medicine must continue to be embedded within the context of clinical trials, and integrated with scientific and clinical collaborative structures to deliver measurable benefits to patients."

More information: www.thelancet.com/journals/lan … (13)70611-9/abstract

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