New way discovered to predict which breast cancer patients should be treated with anthracyclines

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An international team of researchers has discovered a new way of detecting which breast cancer patients are going to respond best to chemotherapy that includes anthracycline antibiotics.

The research, presented at the seventh European Breast Cancer Conference (EBCC7) in Barcelona today (Thursday), is important because, until now, there was conflicting evidence about the best way of predicting response to anthracyclines and it was unclear whether any of the known biomarkers, such as the genes HER2 and TOP2A, were accurate indicators of response to these drugs.

By conducting a meta-analysis of four large breast cancer trials including nearly 3,000 patients, the researchers have discovered that an abnormality on chromosome 17, called CEP17, is associated with a worse outcome for patients, but also that its presence is a highly significant indicator that the tumour will respond to anthracyclines.

After adjusting for additional factors relating to the tumour and its treatment, the researchers found that if patients with CEP17 were treated with anthracyclines, they were approximately two-thirds more likely to survive and to survive without a recurrence of cancer than those who did not receive anthracyclines (recurrence free survival was 67% and overall survival was 63%).

John Bartlett, Professor of Molecular Pathology at the University of Edinburgh (Edinburgh, UK), said: "Our aim was to identify patients for whom anthracyclines provided benefit in terms of disease control and increased survival, and to seek to ensure that future treatment was targeted to this group. Our finding that patients whose tumours have the CEP17 abnormality are more likely to respond to anthracyclines is entirely novel. Subject to confirmation, this suggests that only those patients with CEP17 tumours should receive anthracyclines, thereby enabling other patients who do not have the CEP17 abnormality to avoid a toxic treatment that will not be effective."

CEP17 is on the same chromosome as two other genes known to be involved in breast cancer, HER2 and TOP2A, but the researchers did not find any significant associations between them and response to anthracycline treatment.

The discovery may open the way not only for clinicians to give anthracycline treatment to patients who will benefit the most from it, but also for biochemists to research the mechanisms involved in CEP17 and to design new drugs to target these pathways.

Prof Bartlett said: "We need to understand what CEP17 is telling us about the behaviour of breast cancer cells. It works as a biomarker for predicting response to anthracyclines, but we don't know why it works. So our next step is to discover this and to try to make the cancers that don't have the marker behave like the ones that do, so that they will respond to anthracyclines."

CEP17 is detected by a common and straightforward test (fluorescent in situ hybridisation or FISH), which is carried out routinely in breast cancer patients; it is used to test for the HER2 gene to see whether the women might benefit from the drug Herceptin. Prof Bartlett said that assessment for CEP17 could be easily carried out in the same FISH

analysis as for HER2.

He concluded: "This is the largest study of its kind, with consistent results across multiple trials, and it provides a unifying hypothesis for previous conflicting data."

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