Thursday, 12 February, 2015

In Europe, some 463 000 women are diagnosed with breast cancer each year, making it the most common form of cancer in women. Depending on certain conditions, different drug combinations will be more – or less – effective. The EU-funded RESPONSIFY project has identified these conditions. Their findings could help physicians tailor treatment to individual patients, avoiding ineffective therapies. The researchers are now working towards further clinical trials.

In breast cancer treatment, tumours tend to respond differently to different drugs, including carboplatin, trastuzumab and lapatinib. However, markers showing the potency of each of these drugs on specific patients, known as clinical assays, are lacking. Knowing their impact on defined patient groups would save lives by helping doctors administer the most effective therapy faster. It would also spare patients unnecessary and unpleasant side effects.

RESPONSIFY has developed biomarker tests that look at the tumour's molecules to assess the profile of a patient’s cancer. The results show how individuals may respond to specific cancer treatments.

**When drugs work – and when they don’t**

“We ran clinical trials on several hundred breast cancer patients,” says RESPONSIFY project coordinator Carsten Denkert from Charité University in Berlin, Germany. “The team gained valuable insights into which women were, and weren’t, responding to different drug combinations.”

The researchers studied the effects of the drug combinations on the tumour before surgery. This so-called ‘neoadjuvant therapy’ aims to reduce the size or extent of tumours before surgeons operate. Its effects are immediately visible, giving doctors a prognosis and treatment strategy much earlier than was previously possible.

The team found that the neoadjuvant drug carboplatin works well in patients that have many inflammatory (immune) cells located inside their tumour. This information tells doctors that the patient is likely to react well to chemotherapy, with the body's own defences supporting and
Resistance genes

Some 15 to 30 % of breast cancers have an excess of HER2 - a protein that promotes the growth of cancer cells. The RESPONSIFY researchers examined how changes in the tumour's DNA, known as gene mutations, can hamper breast cancer therapy. They found that certain mutations of the 'PIK3CA gene' resulted in resistance to the combined anti-HER2 therapies of trastuzumab and lapatinib. This tells doctors that patients with this mutation might not benefit from these drug combinations. Armed with information on a patient's PIK3CA gene, doctors will be able to find the right drugs faster.

“This targeted and personalised approach could improve quality of life for women diagnosed with breast cancer, who would be given optimal treatment in the right doses. Given the high cost of cancer drugs, it would also ease the burden on healthcare systems,” adds RESPONSIFY's scientific coordinator, Sibylle Loibl from the German Breast Cancer Group.

The project's SME partners have considerable expertise in developing biomarker tests and according to Denkert, standardised biomarker assays could be available in “some years”, once further clinical trials have taken place.

To reach this point, the partners are continuing their research with funding from various research agencies.

Below image of breast carcinoma with an increased infiltrate of immune cells. Tumors with this morphology often shown an increase response to therapy.

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See also:
CORDIS [3]

Project:
Genome-based biomarkers leading to validated molecular diagnostic tests for response prediction in breast cancer
**Project Acronym:**
RESPONSIFY

**Project website:**

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