Biomarkers uPA/PAI-1 in breast cancer: Benefit and harm of the test unclear

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To make a decision for or against adjuvant chemotherapy, a test to measure the concentrations of the biomarkers uPA and PAI-1 in the tumour tissue is available for breast cancer patients. However, as suitable studies are lacking, it remains unclear for patients with an intermediate risk of recurrence which benefit or harm a treatment strategy based on this test may have for them. This is the result of the final report published by the Institute for Quality and Efficiency in Health Care (IQWiG) on 20 October 2014.

Adjuvant systemic treatments aim to prolong survival

Even if the breast cancer was completely removed in surgery, the tumour can come back. The risk of such a recurrence can be low, intermediate or high. Adjuvant systemic treatments including chemotherapy are used to lower the risk of recurrence and prolong survival. Until now, whether or not they are used has mostly been determined by the patients' age, the number of lymph nodes affected and the grade of the tumour cells.

Predictive markers aim to improve treatment decision

Whereas generally no chemotherapy is recommended for patients with low risk of recurrence, doctors usually recommend adjuvant treatment for patients with high risk of recurrence. However, for patients with an intermediate risk, the established factors (including grade of the tumour cells) are not sufficient to make such a treatment recommendation. This

is why the guidelines do not contain any such recommendations.

In order to make better treatment decisions in patients with intermediate risk of recurrence, and to potentially spare them from the burden of chemotherapy, researchers are investigating so-called biomarkers. These biomarkers aim to help identify those patients who are very likely to benefit from chemotherapy.

High concentration is associated with poor prognosis

The two proteins urokinase-type plasminogen activator (uPA) and its inhibitor PAI-1 could be this kind of biomarkers. Both play an important role in metabolic processes taking place in the tumour. If their concentration in the tumour tissue is high, there is also a higher probability of recurrence.

IQWiG was commissioned to investigate whether uPA and PAI-1 are also suited as so-called predictive markers and whether treating staff and patients can base their decisions for or against chemotherapy on the results of corresponding tests.

Design of the only study was unsuitable

IQWiG found one study (the Chemo N0 study) that investigated the benefit of adjuvant chemotherapy in patients with high concentrations of uPA and PAI-1. However, its design was unsuitable to comprehensively answer the research question of the report.

On the one hand, patients with high concentration of the marker who received chemotherapy had no survival advantage (disease-free survival and overall survival) in comparison with patients without chemotherapy. On the other hand, the benefit of chemotherapy was not investigated in

patients with low concentration of uPA and PAI-1.

As suitable studies are lacking, the benefit or harm of a strategy based on uPA and PAI-1 for or against chemotherapy therefore remain unclear.

Provided by Institute for Quality and Efficiency in Health Care