Urokinase-type plasminogen activator (uPA) and its inhibitor PAI-I: novel tumor-derived factors with a high prognostic and predictive impact in breast cancer.

Abstract:
Urokinase-type plasminogen activator (uPA) and its inhibitor, PAI-I, play a key role in tumor invasion and metastasis. They were the first novel tumor biological factors to be validated at the highest level of evidence (LOE I) regarding their clinical utility in breast cancer. Their antigen levels are determined in tumor tissue extracts by standardized, quality-assured immunometric assays (ELISA). Since the late 1980s, numerous independent studies have demonstrated that patients with low levels of uPA and PAI-I in their primary tumor tissue have a significantly better survival than patients with high levels of either factor. These prognostic data have recently been validated by an EORTC (European Organization for Research and Treatment of Cancer) pooled analysis comprising more than 8,000 breast cancer patients. In addition, results from a multicenter prospective randomized therapy trial in node-negative breast cancer (“Chemo N(0)”) showed that node-negative breast cancer patients with low levels of uPA and PAI-I in their primary tumor have a very good prognosis, and may thus be candidates for being spared the burden of adjuvant chemotherapy. In contrast, node-negative patients with high uPA/PAI-I are at substantially increased risk of disease recurrence, comparable to that of patients with three or more tumor cell positive...
axillary lymph nodes. The "Chemo N(0)" trial as well as retrospective data also indicate that these high-risk patients benefit from adjuvant chemotherapy. In conclusion, over a period of about 15 years sufficient evidence has been put forward to demonstrate that determination of uPA and PAI-I in primary breast cancer patients supports risk-adapted individualized therapy decisions, particularly in patients with node-negative disease.