Prognostic significance of urokinase-type plasminogen activator (uPA) and plasminogen activator inhibitor (PAI-1) in patients with primary invasive ductal breast carcinoma – a 7.5-year follow-up study

Sanda Jelisavac-Cosic¹, Maja Sirotkovic-Skerlev^{1,4}, Ana Kulic¹, Jasminka Jakic-Razumovic^{2,4}, Zdenko Kovac^{1,4}, and Damir Vrbanec^{3,4}

¹Department of Pathophysiology, ²Department of Pathology, and ³Department of Oncology, Zagreb University Hospital, Zagreb; ⁴Zagreb University Medical School, Zagreb, Croatia

ABSTRACT

Aims and background. Urokinase-type plasminogen activator (uPA) and plasminogen activator inhibitor (PAI-1) are key molecules in pericellular proteolysis, a process that plays an important role in tumor invasion and metastasis. In the current study we investigated the prognostic significance of uPA and PAI-1 in primary invasive breast cancer.

Methods and study design. uPA and PAI-1 antigen levels were determined by enzyme-linked immunosorbent assay in cytosols of 177 invasive ductal carcinoma specimens. The prognostic significance of uPA and PAI-1 was assessed for overall survival. The median follow-up time was 90 months.

Results. In univariate analysis, both uPA (third *versus* first tertile range of values; P = 0.02; HR = 2.08) and PAI-1 (third *versus* first tertile; P = 0.0007; HR = 3.1) were significant prognostic markers for overall survival. In multivariate analysis only nodal status (N2 vs N0; P = 0.0001; HR = 3.94) and PAI-1 (third *versus* first tertile; P = 0.004; HR = 3.05) remained significant independent prognostic factors. Both uPA and PAI-1 were correlated with established prognostic markers including histological grade, tumor size and Nottingham index.

Conclusion. Our study with a 7.5-year follow-up confirmed the relation between elevated uPA and PAI-1 values and an aggressive course of invasive breast cancer. The prognostic significance of PAI-1 as an independent marker was proved for the overall group of breast cancer patients and the subgroup of node-positive patients.

Key words: breast cancer, urokinasetype plasminogen activator (uPA), plasminogen activator inhibitor (PAI-1), survival analysis.

Conflict of interest: None declared.

Acknowledgments: The authors wish to thank the Croatian Cancer Registry for their kind help in providing our team with the data on the overall survival of our patients.

Correspondence to: Sanda Jelisavac-Cosic, MSc, Department of Pathophysiology, Zagreb University Hospital, Kispati eva 12, 10000 Zagreb, Croatia. Tel +385-91-8961683, +385-1-2367294; fax +385-1-2367283;

e-mail jelisavaccosic.sanda@gmail.com

Received August 2, 2010; accepted April 15, 2011.