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Objective: Estrogen receptor α (ERα) is a member of the nuclear receptor family. Over 70% of breast cancers are ERα-positive, and endocrine therapy targeting estrogen action decreases mortality from breast cancer. Recently, a novel protein kinase that regulates ERα activity, lemur tyrosine kinase-3 (LMTK3) has been identified. In this study, we investigated whether *LMTK3* mRNA expression and its polymorphisms are associated with prognosis in breast cancer patients during long-term follow-up.

Methods: First, we investigated the relationship between mRNA expression of *LMTK3* and patient outcome in 219 breast cancers. The effects of several variables on survival were tested by Cox proportional hazards regression analysis. Next, we performed *LMTK3* genotyping in 471 breast cancers to clarify the prognostic role of these polymorphisms.

Results: Our data showed that *LMTK3* expression level was not associated with prognosis in all patients. We then analyzed the impact of *LMTK3* mRNA expression on the prognosis of breast cancer according to ERα status. Both disease-free survival and overall survival were significantly shorter in ERα-positive patients with high *LMTK3* expression receiving adjuvant endocrine therapy than in those patients with low *LMTK3* expression. Multivariate Cox regression analysis revealed that high *LMTK3* expression was an independent poor prognostic factor in ERα-positive breast cancer patients. We did not find any correlation between *LMTK3* genotypes and prognosis of breast cancer patients in our series.

Conclusions: Our results show that high expression of *LMTK3* is an independent prognostic factor in ERα-positive breast cancer patients receiving adjuvant endocrine therapy.