

# SERUM THYMIDINE KINASE 1 ACTIVITY IN BREAST CANCER

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## INTRODUCTION

Thymidine Kinase 1 (TK1) is an enzyme involved in DNA synthesis by incorporating thymidine and, therefore, is considered to be an important proliferation marker. The recently developed high-sensitive assay DiviTum® has a much higher analytical sensitivity for TK1 activity than previous assays. This allows detecting even small changes in proliferation activity of malignant tumor disease.

## STUDY AIMS

To characterize the association of circulating TK1 with the main clinicopathological parameters in breast cancer (BC). To estimate the predictive value of TK1 for disease recurrence after surgery.

## PATIENTS AND METHODS

IRB approved protocol. HMO-0441-08.

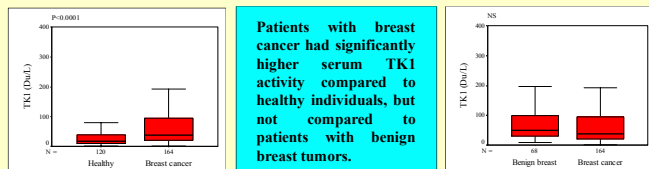
Study design. A. Healthy - 120; B. Benign breast tumors - 68. C. Operable BC - 165.

Methods. Serum TK1 activity was measured preoperatively by ELISA kits: DiviTum® (Biovia, Sweden).

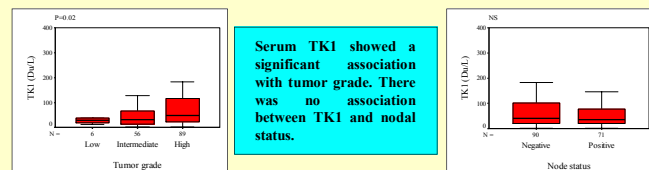
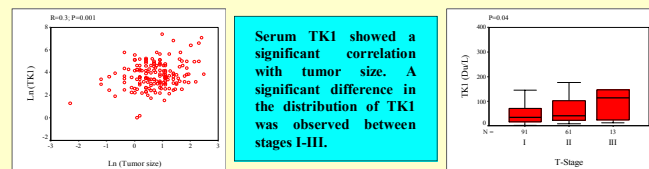
Statistics. Non-parametric tests were used for comparisons between numeric variables. For analyses of the sensitivity-specificity relation of the assays, receiver operating characteristic (ROC) curves were constructed, and the areas under these curves (AUC) were calculated. The models for the probability of disease recurrence as a function of the serum TK1 activity were constructed using logistic regression analysis. A value of  $P < 0.05$  was considered significant.

## RESULTS

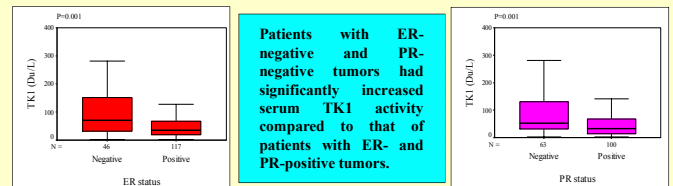
### Association of TK1 with tumor stage, grade and nodal status



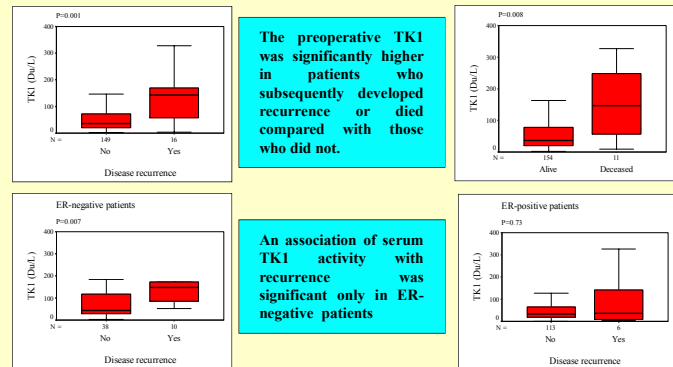
Patient characteristics (n=165)		
Age, years	Median (range)	57 (24-83)
Histology	IDC/ILS/Others	146 / 14 / 5
T-stage	I / II / III	91 / 61 / 13
N-status	Yes / No / nd	90 / 71 / 4
Grade	I / II / III / nd	6 / 56 / 89 / 14
ER-status	Yes / No / nd	117 / 46 / 2
PR-status	Yes / No / nd	100 / 63 / 2
HER2-status	Yes / No	27 / 139
Follow-up, months	Median (range)	44 (13-65)



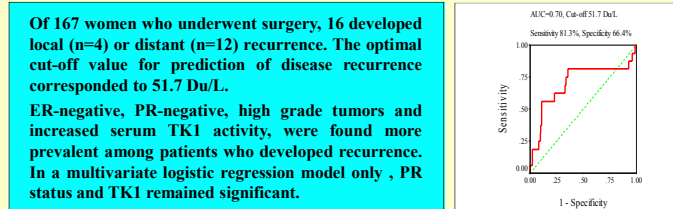
### Association of TK1 with ER- and PR-status



### Association of TK1 with outcome



### TK1 in recurrence prediction



Parameters	Univariate analysis		Multivariate analysis		
	No. of pts	No. of pts with recurrence (%)	P Value	Odds Ratio (CI)	P Value
Grade					
Low	62	2 (3.2)	0.02	1	0.27
High	89	14 (15.7)		2.6 (0.5-13.5)	
ER-status					
Pos	117	6 (5.1)	0.003	1	0.7
Neg	46	10 (21.7)		1.5 (0.2-10.2)	
PR-status					
Pos	100	4 (4.0)	0.002	1	0.02
Neg	63	12 (19.1)		4.5 (1.3-15.3)	
TK1 (Du/L)					
≤51.7	98	3 (3.1)	0.0007	1	0.004
>51.7	66	13 (19.7)		7.2 (1.9-27.3)	

## CONCLUSIONS

Preoperative serum TK1 activity in BC patients is significantly associated with tumor size, grade, ER-, PR-status and disease outcome.

Preoperative measurement of serum TK1 activity may help in predicting of disease recurrence.