Abstract Number: 2558
Presentation Number: PS3-10-20

TREC and KREC Levels as Immunological Markers for Predicting Recurrence in Early Breast Cancer

Objective

To improve the treatment outcomes for patients with malignant neoplasms by using the assessment of T-cell Receptor Excision Circles (TREC) and K-deleting Recombination Excision Circles (KREC) levels for planning and conducting systemic anticancer drug therapy, specifically in early breast cancer.

Materials and Methods

•**Study Population:** The study included 196 primary female patients (aged 26-91, median 53) with early-stage (I-III) luminal HER2-negative breast cancer and a control group of 213 healthy adult donors.

•**Methods:**

- Blood was collected before the start of adjuvant therapy.
- **TREC and KREC levels** were quantified in peripheral blood using real-time PCR with the "IMMUNO-BIT" reagent kit.
- Routine laboratory tests (complete blood count, biochemistry) were performed.
- Germline and somatic mutations in *BRCA1/2* genes were analyzed using allele-specific PCR and Next-Generation Sequencing (NGS).
- Statistical analysis was performed using StatTech v.4.6.1, including descriptive statistics, correlation/regression analysis, ROC analysis, and Cox proportional hazards regression.

Results

•**TREC vs. Healthy Donors:** Breast cancer patients had statistically significantly lower median TREC levels (18.62 copies/10^5 cells) compared to healthy donors (73.50 copies/10^5 cells), indicating T-cell immunodeficiency.

•**Age Dependency:** A significant inverse correlation was found between TREC levels and patient age. TREC levels decreased progressively across age groups (25-44, 45-60, >60 years). KREC levels showed no significant correlation with age.

•**Cancer Stage:** Patients with more advanced disease stages (III) had lower median TREC levels (Stage I: 20.70, Stage II: 18.62, Stage III: 12.88 copies/10^5 cells), though the differences were not statistically significant. KREC levels showed no significant variation across stages.

•**Recurrence Prediction:**

- Patients with disease recurrence (n=21) had significantly lower median TREC levels (3.0 copies/10^5 cells) than those without recurrence (22.43 copies/10^5 cells).
- ROC analysis for TREC yielded an AUC of 0.822. A TREC cut-off value of **11.31 copies/10^5 cells** predicted recurrence with 85.7% sensitivity and 72.6% specificity.
- KREC levels were not a statistically significant predictor of recurrence (AUC=0.588).

•**Cox Regression:** Multivariate analysis confirmed that a lower TREC level was a significant independent factor for increased recurrence risk (HR 0.931, p=0.007).

Conclusion

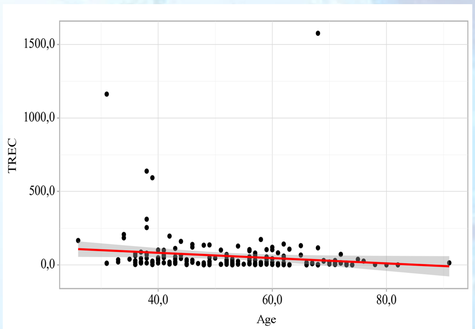
The level of TREC, a marker of T-cell neogenesis and thymic function, is significantly reduced in breast cancer patients compared to healthy donors and is inversely correlated with age and disease stage. A low TREC level (< 11.31 copies/10^5 cells) is a strong and significant predictor of an increased risk of breast cancer recurrence. Monitoring TREC levels provides a valuable immunological tool for risk stratification and could guide personalized adjuvant treatment decisions, such as the addition of CDK4/6 inhibitors for high-risk patients. In contrast, KREC (a B-cell marker) showed limited prognostic value in this context.

Impact of Individual Factors on Recurrence Risk in the Breast Cancer Cohort

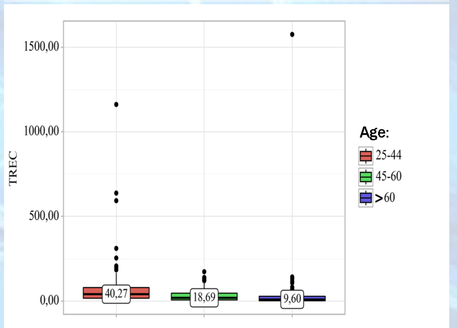
Risk Factor	Unadjusted (Crude) Hazard Ratio		Adjusted Hazard Ratio	
	HR; 95% ДИ	P	HR; 95% ДИ	P
TREC	0,928; 0,883 – 0,976	0,004*	0,931; 0,884 – 0,981	0,007*
Stage II	36401784,157; 0,0 – inf	0,995	32982320,966; 0,0 – inf	0,994
Stage: Stage III	137497283,2; 0, 0 – inf	0,994	89248459,128; 0, 0 – inf	0,994
KREC	1,0; 0,999 – 1,0	0,580	1,0; 1,0 – 1,0	0,84

Note: HR – Hazard Ratio; * – differences are statistically significant (p < 0.05).

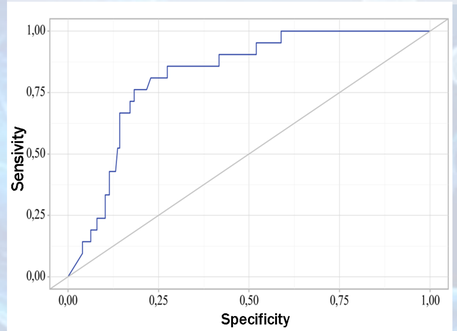
Scatter Plot with Regression Line Showing TREC by Age in Breast Cancer Patients



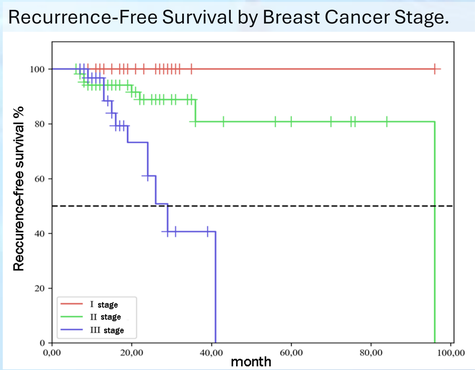
TREC Levels by Age Group in Women with Breast Cancer



ROC Curve for Predicting Recurrence Based on TREC Levels in Women with Breast Cancer



Recurrence-Free Survival by Breast Cancer Stage.



Authors: Aleksandr V. Sultanbaev, Irina A. Tuzankina, Irina V. Kolyadina, Nadezhda I. Sultanbaeva, Ainur F. Nasretdinov, Konstantin V. Menshikov, Shamil I. Musin, Mikhail V. Sultanbaev, Dmitriy A. Kudlay

Center:
Federal State Budgetary Institution of Science Institute of Immunology and Physiology of the Ural Branch of the Russian Academy of Sciences, Yekaterinburg, Russian Federation; State Autonomous Healthcare Institution Republican Clinical Oncological Dispensary of the Ministry of Health of the Republic of Bashkortostan, Ufa, Russian Federation; Department of oncology, Russian Medical Academy of Continuous Professional Education, Moscow, Russian Federation; Department of Pharmacognosy and Industrial Pharmacy, Lomonosov Moscow State University, Moscow, Russian Federation.

Corresponding author:
Alexander V. Sultanbaev, rkodrb@yandex.ru