

in each group was calculated. Tumor multiplicity was defined as the average number of tumors per mice, obtained by dividing the total number of tumors by the total number of mice per group, including non-tumor bearing animals.

Bronchoalveolar lavage (BAL) of lungs was performed on 6 mice (animals were anesthetized by an ip injection of sodium thiopental) from each study group at the 1, 7, 15 and 30 days after irradiation and SO<sub>2</sub> inhalation. Total cells of BAL were counted using hemocytometer chamber and an optical microscope with a 400× zoom. BAL differential cell (macrophages, lymphocytes, eosinophiles and neutrophils) counts were performed on slides (Romanowsky stain). Phagocytic activity of AM was counted on slides. AM morphometric study was done by measuring the area of each cell (square of cell) and the area of nuclear of each cell (square of nuclear) with use of the original image analyzer computer system.

**Results:** Results of the combined effects of radiation and inhalation of sulfur dioxide showed the growth of tumor quantity in the lung: the frequency of adenomas/mouse was more than 42% higher than that of control group. Synergism coefficient was 1.1 in this case.

Irradiation at a dose of 1.0 Gy modifies the reaction of free cells of lung on the action of sulfur dioxide, which is manifested in the change of the number of cells in the BAL fluid, the phagocytic activity of the AM, as well as of the changes the morphometric parameters of their cells.

**Conclusion:** Thus, if the amount of radiation exposure of BAL cells was significantly reduced by the 1st and 7th days, and after inhalation of sulfur dioxide – tended to increase, then the combined action on the 7th day it was almost half the theoretical (hypothetical) the sum of the separate effects of the studied factors. Exposure to sulfur dioxide significantly slowed the activation of cell count. It was found, that after combined action of the investigated factors the morphological characteristics of macrophages (reducing the square of cells and their nuclei) have changed (7th and 15th day). The absorption activity of phagocytes was significantly reduced (7 day).

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## T15

### Circulating tumor cells and bone marrow progenitor cells in the blood of breast cancer patients in the dynamics of neoadjuvant chemotherapy

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**Background:** Despite the abundance of theoretical evidences displaying the considerable role of the “soil” in metastasis progression, the majority of cancer research and cancer therapy

pathogenetic methods focused mainly on the tumor cells. There is still no clear clinical data showing the role of “soil” in the metastasis. Identification of factors and mechanisms driving the conditions promoting tumor dissemination may lead to therapeutic strategy to detect and prevent metastases at the earliest step. It has been established that bone marrow-derived hematopoietic progenitor cells home to pre-metastatic sites before tumor cells infiltrate in these sites. These hematopoietic progenitor cells form regulatory cell cluster of stromal microenvironment (premetastatic niche) to promote secondary tumor growth. In this context, the aim of our study was to evaluate the level of different pools of circulating tumor cells and bone marrow progenitor cells in the blood of patients with breast cancer in the dynamics of neoadjuvant chemotherapy.

**Materials and methods:** Patients (prospective study) with newly diagnosed invasive breast cancer in the age range 18–50 years and tumor volume of 2.0(> or =) cm, referred at the Tomsk Cancer Research Institute for treatment were included into the study. Eligibility criteria were as follows: the patient's informed consent to participate in research; morphologically verified diagnosis of invasive carcinoma of non-specific type; luminal B-1, -2, triple negative (basal-like subtype included), HER2 positive breast cancer; T2-4N0-3M0; preserved menstrual function; satisfactory performance status (on a scale (< or =) ECOG 2). Exclusion Criteria were: other than luminal histological type of breast cancer, multiple primary cancer; chronic inflammatory diseases in the acute stage. Samples of venous blood taken from breast cancer patients before biopsy, after biopsy and after each subsequent course of neoadjuvant chemotherapy (NACHT) were served as a study material. The various pools of circulating tumor cells and bone-marrow derived progenitor cells were determined using monoclonal antibodies to EpCam, CD44, CD45, CD24, N-cadherin, CD34, CD133, CD202, VEGFR1 and CD90, labeled with different fluorochromes on flow cytometry BD FACSCanto™ II.

**Results:** The study showed that each succeeding course of NACHT increased blood levels of circulating tumor cells, and bone marrow progenitor cells with a phenotype characteristic of EPC (endothelial progenitor cells) (CD34 + CD45-VEGFR + CD133 + CD202 +) and MSC (mesenchymal progenitor stem cells fibroblasts) (CD34-CD90 + VEGFR1-CD45-CD202-). Influence of the NACHT on hematopoietic stem cells HSC (VEGFR1 + CD34 + CD45lowSD202-) and progenitor cells HPC – CD34 + CD45 + CD90-VEGFR1 + CD133 – was ambiguous.

**Conclusion:** Neoadjuvant chemotherapy increases blood levels of circulating tumor cells, endothelial progenitor cells and mesenchymal stem cells progenitor fibroblasts, thus promoting the formation of premetastatic niche.

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