

## Immediate Results of the Treatment of Breast Cancer of Stages 1-2 with the IHC

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Over the past few years the significant progress has been achieved in the clinical use of various biological markers. These include oncogenes, estrogen receptors (ER) and progesterone (PR), markers of apoptosis, growth factor receptors, etc. These figures allow to study in more detail molecular biological characteristics of malignant tumors, associated with the degree of differentiation, the ability to invade and metastaze, chemotherapy sensitivity, and hence a specific course and prognosis of the disease in each concrete case. Current approaches to the treatment of patients with breast cancer suggest an individualized choice of the type of treatment, taking into account the risk category and sensibility of tumor cells to hormone therapy. It should be noted that modern selection of adjuvant therapy depended on the extent of the primary tumor and its histological grade of malignancy, the level of expression of steroid hormone receptors, reproductive status and age of the patients. But in recent years the attention of scientists and clinicians focused on the molecular biology of tumor markers, such as Her-2/neu. PR is the first vital link cell responses to progestines. Their synthesis in tumor cells of the mammary gland is induced with estrogens (i.e., the presence of PR indicates to the functional activity of estrogen), the presence of ER in the tumor points to its potential sensitivity to drugs of antiestrogene series, medical or surgical castration. Hormone-dependent tumor of the mammary gland containing one or both reseptors has more favorable course and prognosis.

Oncomarker Her2/neu is the receptor of the human epidermal growth factor protein found in normal cells and epidermal origin and it is involved into the activation by regulating the normal growth and development of gland tissue. Disregulation of these processes can lead to malignant transformation, which becomes apparent hyperexpression and application of Her-2/neu. Currently, clinics and laboratories use a large arsenal of diagnostic methods . Thus to determine the hormonal status of the mammary tumors in equal measure there are used three methods: radioligand, immunofermental and immunohistochemistry (IHC).

Immunohistochemical method with the highest circulation in practice, has become the "gold standard" in the definition of estrogens receptors, progisterone receptors and Her2/neu and oncoprotein in breast cancer cells. The method allows to determine the percentage of positive cells, to assess the extent and intensity of the reaction to give a precise formulation, characterization of the tumor. However, along with the advantages it has several disadvantages such as: loss of antigen and masking the preparation of drugs, a long time of molecular markers determination, as well as generally, the present study is carried out after the surgery, when the entire tumor is removed. Prior to operating IHC study was performed on the tissue columns obtained at trepanobiopsy.

In patients with breast cancer the definition particularly of hormone and drug sensitivity of tumors is actual for individual selection regimens. The results are achieved with endocrine therapy of breast cancer with ER+– and PR+– status better than with other variants of receptor phenotype. Receptor-positive breast tumors have higher and more favorable differentiation and clinical course. Her 2 - positive breast cancer is a particular form of cancer that requires specific and urgent treatment because of their rapid growth. For this reason it is very important as soon as possible after diagnosis to determine the receptor status and not to delay the study until the relapse or progression of the disease.

**The aim** of our study is to analyze the results of breast cancer in the Amur Region, taking into account the data of IHC. 70 cases of patients with breast cancer of the stage 1-2 treated during the year (June 2011-July -2012) were taken for the study.

Characteristic of patients with breast cancer according to stages was: Stage 1 (T<sub>1</sub>N<sub>0</sub>M<sub>0</sub>) – 14 people (20%), II A-B (T<sub>0</sub>N<sub>1</sub>M<sub>0</sub>, T<sub>1-2</sub>N<sub>1</sub>M<sub>0</sub>, T<sub>2-3</sub>N<sub>0</sub>M<sub>0</sub>) – 56 people (80%). Thus the bulk of the patients with II-stage (80%) made up the main contingent, and only 20% were in stage I.

Characteristic of patients with breast cancer according to forms: low differentiated cancer made up-19 (27%), undifferentiated cancer - 45 (64%), well-differentiated cancer - 6 (9%). In all there were 70 patients. A retrospective analysis of morphological findings showed that the majority of tumors was of an undifferentiated structure (64%), which describes the characteristic of the disease and the difficulty of diagnosis.

The distribution of patients depending on the hormonal status of the tumor was: ER-hormonal status ER(+) PR (+) -10(14%), ER(+) PR(-)-6(9%), ER(-) PR(+)-45(64%), ER(-) PR(-)-9(13%), a total number was 70 cases, according to HER 2/neu-status: HER 2/neu (+)- 20(29%), HER 2/ neu(-) - 50(71%) of 70; triplenegative group - HER 2/neu (-), ER(-), PR(-)-6(9%).

The distribution of patients according to the target therapy: Group 1 included patients with positive hormonal status of breast tumor in all variants of the receptor phenotype (either both "+" - ER + PR + or one of them - ER (+) PR (-), ER (-) PR (+) was 87%. Taking this group as a single whole 20% have HER 2/neu (+), and therefore Herceptin with hormonal therapy was included into medicamentous therapy (antiestrogens: Arimidex, Tamoxifen for a long time); with an aromatase inhibitor medicamentous or surgical castration was performed in rare cases. The remained 80% of patients with HER 2/neu (-) in combination with medicamentous or surgical castration received an anti-estrogen treatment). And the percentage of castration of the patients was only 25% and was in the group with hormonopositive status, 21% of which was performed surgical castration and 4% of cases received medicamentous castration (Zalodeks); the second group with negative hormonal status and HER 2/neu (+), made up only 6%. The entire group was treated with Herceptin; the third group – 9% with triplexnegative status (HER 2/neu (-), ER (-) PR (-), besides surgical and radial therapy received a course of medicamentous therapy according to regimens AC, FAS, taxanes.

Percentage of progression of breast cancer target therapy against the background was only in the group of patients with positive hormonal status of the tumor and made up 10% (7 people). Let's consider this fact in detail. Patients with HER 2/neu (+) with mts in the lungs (1), brain (1) received Herceptin with positive changes (i.e. reduction of the size of the lesion); patients with HER 2/neu (-): with mts in the lungs (3), in bones (1) - received polychemotherapy; one patient with postoperative cicatrix was performed dissection.

Side effects and complications: depression of hemopoiesis (leukopenia), hepato and nephrotoxic effects on the background of drug therapy were observed in 15% of patients; post hemorrhagic anemia in the postoperative period was observed in 10% of patients, post radial changes in the respiratory system and skin (post-radial fibrosis, pneumonitis, epidermitis) were in 21% of cases.

**Conclusions.** It becomes increasingly clear that the benefits of adjuvant therapy depends on primarily on the biology of the tumor. Thus tumors with high expression of ER and PR and HER 2 as a rule have the low histological tumor grade and low grade of cellular proliferation, and according to analysis their characterized by the low scale recurrence. Retrospective studies suggest that patients with such tumors do not require adjuvant cytotoxic chemotherapy, which is additional to hormonotherapy. Contrary to this, tumor and progressing hormonoreceptors or the low level of ER and PR, but highly expressing HER 2/neu with the high degree of malignancy and proliferation with high risk scale of relapse as a rule are resistant to hormonotherapy, but they are sensitive to chemotherapy, while HER 2 positive tumors are resistant to adjuvant therapy with Herceptin. The analysis of the effectiveness of adjuvant hormonal therapy and chemotherapy confirms our opinion that when the role of one of them increases the role of the other reduces. Our research showed that adjuvant hormonal therapy and chemotherapy should be based both on the biological characteristics of the tumor and on its pathomorphological signs. These conclusions apply to adjuvant treatment of early (operable) breast cancer forms. The obtained recently information on the profile of the gene

expression characterizing to therapy and prognosis of the disease evidently intensify the tendency to individualization of planning and performing of adjuvant therapy.

## **Pregnancy and perinatal outcomes in women with a history of ovarian hypofunction**

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**Summary:** 95 pregnant women with a history of ovarian hypofunction (study group) and 30 with normal menstrual cycle (control group) were prospectively examined. Pregnancy had complicated by threatened interruption of placental insufficiency and preeclampsia in the main group. 6.1% of the children were born in asphyxia. The placental growth factor (PIGF), its free receptor (VEGFR-1) and value PIGF/VEGFR-1 were examined in the blood serum of pregnant women, and their levels were lower in the study group compared to the control ( $p < 0.05$ ). It is concluded that the possibility of their value in placental angiogenesis and development of primary placental insufficiency in 8.4% of pregnant women. The content of  $\beta$ -human chorionic gonadotropin ( $\beta$ -HCG), progesterone (PG) and  $\alpha$ -fetoprotein ( $\alpha$ -FP) is lower in the blood of pregnant women in the basic group than in the control, which is typical of placental insufficiency.

**Keywords:** pregnancy, the placenta, placental growth factor, a newborn.

Worldwide the frequency of gynecological diseases among adolescent girls is increasing [1, 14]. Violations of becoming the menstrual function reaches 61 % [11, 15]. The ovarian hypofunction has a value in this disease because of the immaturity of neuroendocrine regulation. Clinical manifestations of ovarian hypofunction are delayed puberty and oligomenorrhea. Violations at the level of the hypothalamic-pituitary axis is one of the causes of endometrial hyperplasi and of disorders of the blood supply to the uterus and ovaries [5, 8, 16]. Women with ovarian hypofunction in the period of menstruation increases the frequency of infertility, miscarriage [9, 13]. In 52.6% of pregnant women formed placental insufficiency due to violation of the quantitative and qualitative relationships between ovarian steroid hormones and their receptors in the endometrium [1, 12].

The ratio of blood flow in the vessels of the uterus affects the willingness of the endometrium for implantation. [8]. Endometrial vascularization associated with the action of sex steroid hormones. Estrogens stimulate the expression of vasculoendotelial growth factors (VEGF) in the endometrium, which is important in the formation of placental bed. [17] Placental insufficiency underlies the development of obstetric complications and perinatal outcomes [6, 10]. The purpose of the study. To study the course of pregnancy and perinatal outcomes in women with a history of ovarian hypofunction who received treatment in adolescence and the reproductive years.

### **Materials and methods.**

125 pregnant women involved in a prospective clinical study, 95 of them had a history of ovarian hypofunction (study group) and 30 - normal menstrual cycle (control group). Newborns of surveyed mothers ( $n = 96$ ) and ( $n = 31$ ) were the respective groups (in groups is one twins). Pregnant women age is  $26,3 \pm 0,9$  and  $24,7 \pm 0,5$  years ( $p > 0.05$ ). Age of menarche is  $15,4 \pm 1,1$  and  $12,6 \pm 0,9$  years ( $p < 0.05$ ) in groups, respectively. 65 pregnant women in the study group had a history of delayed puberty, which characterized by late onset of menstruation and 30 women had not a regular menstrual cycle. All patients were treated in adolescence and childbearing age and examined by us in the planning of this pregnancy. The normal function of the pituitary