

“FTORAFUR” ® - EFFICIENCY CHECKED BY TIME

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ABSTRACT

Currently, drug therapy of malignant tumors has achieved significant success and is an independent method of treating patients with a common tumor process. The best illustration of this is the fact that lengthening life through the use of chemotherapy becomes the rule rather than the exception. New anticancer drugs that have appeared on the market and the study of a large number of new combinations and administration of cytostatics have not supplanted, but rather strengthened the place of 5-fluorouracil synthesized in 1957 by Charles Heidelberger, which is widely used as the first line of chemotherapy in the world today. This drug is included in almost all standard and experimental chemotherapy regimens.

KEYWORDS: chemotherapy, monochemotherapy, polychemotherapy, 5-fluorouracil, tegafur, Ftorafur.

Despite the appearance in the arsenal of oncologists of new methods of both local and systemic effects on the tumor, as well as the improvement of the surgical technique of surgical intervention, systemic chemotherapy is still firmly in the lead as one of the components of the combined and complex treatment of malignant tumors of various localizations.^[1,2]

A characteristic feature and disadvantage are side effects associated with the specificity of the antitumor effect of the drugs, their low selectivity, and the need to maintain a sufficiently high therapeutic dose, that is, all that chemotherapy does when chemotherapy is given.^[11] Therefore, the problem of quality of life of patients in the process of carrying out this type of treatment is of paramount and urgent.^[4]

Undoubted interest is one of the well-known fluoropyrimidines for oral administration - tegafur, which for many years has been widely used in clinical practice. Tegafur is known to be the transport form of 5-fluorouracil.^[5] When taken orally, it has almost 100% bioavailability. Metabolism of the drug occurs in the liver, as well as in the tumor cells with the formation of the main metabolite, 5-fluorouracil.^[3] The pharmacokinetics of tegafur, as well as its fractional oral administration, help to maintain a constant concentration of 5-fluorouracil, similar to that with prolonged intravenous infusion. The occurrence of toxic effects in the process of chemotherapy and after it often serve as an obstacle to the continuation of treatment with due efficacy, requiring correction.^[14] However, the metabolic characteristics of tegafur, namely a high concentration of

5-fluorouracil in the tumor tissue for a long time than in healthy tissues, tissue-specific metabolic pathway with an increase in the concentration of active metabolites in tumor cells without distribution into the systemic circulation with a decrease in cardio and neurotoxicity, allow to treat tegafur for a long time with minimal systemic toxic complications.^[7,8,9,13] The possibility of oral administration, efficacy and low toxicity make it possible to use tegafur as part of drug combinations.^[10]

Colleagues from the Russian Cancer Research Center named after Blokhin N.N., presents the results of treatment of patients with metastatic and locally advanced breast cancer using the tegafur (Ftorafur®) + vinorelbine regimen.^[6] At the same time, complete and partial regression was noted in 37.5% of patients, the control of tumor growth reached 70%, the median time to progression was 7 months. Moreover, the results of the 1st line of treatment were significantly higher than in the 2nd and 3rd (53.8 vs 27.3%). Tolerance was well tolerated.

Tegafur (“Ftorafur” ®) was also used as a radio modifier during radiation therapy. Incorporating into the molecule instead of thymidine, it changes its structure, thus increasing the radio sensitivity of the cell.^[12] Radiation therapy on the background of radio modification was carried out in 460 patients. Tegafur (“Ftorafur” ®), as a radiomodifier, was administered at a dose of 800 mg / day. during the course of radiation therapy. At the same time, a regression of the tumor process was detected by 21% higher compared with monotherapy, as well as good tolerability of the drug.

The aim of our study was to study the drug tegafur ("Ftorafur" ®) in combination with other anticancer drugs on the effectiveness of chemotherapy for locally advanced and metastatic breast cancer. Since 2010, the Department of Chemotherapy and Onco-Sammology of the RSPMCOR of the Ministry of Health of the Republic of Uzbekistan conducted a study of two combinations of anticancer drugs, including tegafur (Ftorafur®), in the treatment of common and metastatic breast cancer in somatically weakened and elderly patients.

In recent years, one of the most actively used and available combinations of anticancer drugs in elderly and somatically impaired patients is a regimen including cyclophosphamide, methotrexate, and 5-fluorouracil. When creating a combination, instead of 5-fluorouracil, tegafur ("Ftorafur" ®) was used. Chemotherapy regimen: - Cyclophosphamide 50 mg / day. inside daily for 3 weeks; - Methotrexate 5 mg / day. inside (2.5 mg 2 times a day), on the 1st and 2nd days of each week; - "Ftorafur" ® 800 mg / m² / day. daily for 3 weeks. It should be noted that the last decade has been characterized by the use of a large number of combinations in malignant breast tumors, including new drugs: paclitaxel, docetaxel, gemcitabine, capecitabine. Despite this, the treatment regimen we study is of undoubted interest for certain groups of patients who do not have the general somatic status that allows for strict regimens for systemic administration. The group included 63 patients with a morphologically confirmed diagnosis and common forms of breast cancer. Evaluated the effectiveness and toxicity of treatment in patients who have not previously received chemotherapy. Patients received 4 courses of therapy. No full effect registered. A partial effect was noted in 32 (52.2%) patients, progression - in 12 (17.4%), progression - in 21 (30.4%) patients. The highest efficiency (65%) was observed in case of metastases to peripheral lymph nodes. In case of liver metastases, an objective effect was detected in 48% of cases, in the lungs in 40%. One patient showed positive dynamics in metastases to the brain. A good regression was also observed on the part of the primary breast tumor. (67%). The duration of the effect was observed from 2 to 8 months. In general, the effectiveness of this combination reaches the effect from 23 to 60%. To illustrate the effect, we present a case of clinical observation.

Patient A., born in 1962 case history No. 4556. Diagnosis: Cancer of the right breast T3I2M1. Metastatic lesion of the right lung.

At admission the patient's condition is satisfactory. Mammography and ultrasound - the volume of the formation of the right breast with axillary lymph nodes. MSCT of the chest - in the right lobe of the lung a high-intensity focus is visualized, with root lymph nodes enlarged. Histological examination - infiltrating breast carcinoma. G3. The patient was given 8 courses

according to the scheme: Cyclophosphamide 50 mg / day orally every day for 3 weeks; - Methotrexate 5 mg / day. inside (2.5 mg 2 times a day), on the 1st and 2nd days of each week; - "Ftorafur" ® 1600mg / day. (800mg x 2 times a day) daily for 3 weeks. With a 2-week interval between courses. The regression of the primary lesion by 70%, MSCT at the site of the primary lesion in the right lung has a lesion of fibrosis, the basal lymph nodes are not enlarged. The patient performed radical mastectomy. In the outpatient period, the patient received 6 courses of chemotherapy with Ftorafur ®, with an interval of 3-4 weeks. Radiation therapy on the scar and lymph flow zone received a radical program. After that, the patient received hormone therapy for 5 years (tamoxifen 20 mg per day). At present, the patient feels satisfactory, no complaints.

Patient N, born in 1968 case history No. 7684. Diagnosis: Cancer of the right breast T4I2M1. Disintegration of the tumor. Metastatic lesion of the liver.

Upon receipt of the patient's condition is satisfactory. Mammography and ultrasound - the volume of the formation of the right breast with axillary lymph nodes. MSCT of the chest - without distinctions. Ultrasound of the liver - multiple liver damage. Mts. Histological examination - intraductal carcinoma of the breast. G3.

The patient underwent palliative amputation of the right breast with lymph node dissection of the axillary lymph nodes. In the postoperative period, the patient received 12 courses of chemotherapy with Ftorafur ® on an outpatient basis, with an interval of 3-4 weeks. Radiation therapy on the scar and the area of the lymph flow received a radical program 6 months after surgery. The patient received hormone therapy (tamoxifen 20 mg per day). 2 years after the end of treatment, multiple metastatic lesions in the bones were found in the patient. The patient received a bisphosphonate treatment - Zometa® Zomedronic acid for 18 months. Currently, the patient is stabilizing the process in the bones and the liver. The patient continues hormone therapy.

Summarizing all the above, it should be noted that the oral drug Ftorafur ® allows you to maintain a constant and optimal concentration of cytostatic in the tumor tissue, thereby ensuring a sufficiently high treatment efficiency with a decrease in systemic toxicity manifestations, thus determining the patient's quality of life. Moreover, taking into account the economic component of treatment, namely, that Ftorafur ® is available to patients of almost all social groups, while not inferior to the effectiveness of treatment compared to modern expensive drugs, it can be considered the drug of choice in both monotherapy and in the mode of polychemotherapy in modern schemes of ablative therapy.

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