ABSTRACT
To study efficiency of the combined treatment of advanced gastric cancer with inclusion Trastuzumab.

Material: We present the intermediate analysis of the use of target therapy with Trastuzumab in patients with a HER2-positive gastric cancer. Up to 01.10.2009y 118 patients have been tested for HER-2 expression, and in 24 gastric cancer patients it is revealed HER2-positive status of tumor. It is lead chemotherapy to all patients by the PLF regimen and Herceptin in dose 6 mg/kg once in 3 weeks (6 cycles). In control group in 26 patients it is lead only chemotherapy by the PLF regimen once in 3 weeks without addition Trastuzumab (6 cycles).

Results: At the moment of the analysis of preliminary data, the median remission duration in compared groups has made 8.3 months, and 5.2 months, accordingly.

Conclusion: At advanced gastric cancer with high level HER-2 expression Trastuzumab increases frequency of objective effect and the median remission duration.

UDC Code & KEYWORDS
- 616-006 ■ STOMACH CANCER ■ CHEMOTHERAPY ■ TARGET THERAPY ■

INTRODUCTION
Despite of stable decrease in disease and lethality owing to stomach cancer in the West, in eastern countries including in Uzbekistan, this problem remains rather actual [1,2,4,9]. Annually in the world it is diagnosed more than 1 000 000 new cases of this disease. All over the world among the reasons of death from oncological diseases, stomach cancer takes the second place. Early diagnostics is complicated, that is connected with asymptomatic current of this form of cancer at early stages. The analysis of statistics of oncological disease in the CIS countries testifies to increase in contingent of patients with III-IV stages for last years [1, 2, 3].

Till now hopes for treatment of patients suffering from stomach cancer are connected with an opportunity of performance of radical operation. Unfortunately, more than 75 % of primarily revealed patients of disease is registered in III-IV stages. However, in opinion of the majority of authors the problem on expediency of surgical treatment of patients suffering from stomach cancer of IV stage remains unsettled [2, 4, 10]. If at advanced process the majority of surgeons adhere to active tactics revealing of the remote metastases in liver, peritoneal dissemination or metastases in paraaortal lymph nodes quite often forces to refuse attempt of performance even palliative interventions [6, 9].

Thus, the significant group of patients suffering from stomach cancer can hope only on chemotherapy. Advanced stomach cancer is characterized by the adverse prognosis; at application of modern means of therapy average life expectancy of patients after statement of the diagnosis is about 10 months [1, 2, 5].

Development of new modes of the combined chemotherapy with using of preparations influencing growth factor and tumor angiogenesis opens new opportunities in treatment of this pathology. Perspective and poorly studied in treatment of stomach cancer is target therapy [8].

The first information about using of target therapy on stomach cancer was shown with ToGA trial (2008). The given researches of ToGA presented at annual conference of the American Society of Clinical Oncology (ASCO), Orlando, Florida, showed, that addition of Trastuzumab to standard chemotherapy allows to increase survival with this aggressive form of cancer on the average by 3 months. Information of this international trial, phase-III also have shown, that in comparison from patients with the advanced or inoperable HER2-positive stomach cancer, not received Trastuzumab, at patients, its received, the risk of death decreases on 26 %. Expression of HER-2 is observed approximately in 22 % cases of stomach cancer. This parameter is identical both in Europe, and in Asia where stomach cancer occurs very often [7, 8, 10].

Proceeding from above stated, the purpose of the present research was studying of HER-2 among patients with the advanced stomach cancer of Uzbek population and preference of the combined mode with inclusion Trastuzumab in comparison with chemotherapy.

MATERIALS AND METHODS
We represent the intermediate analysis of using of target therapy with Trastuzumab among patients with HER2-positive advanced stomach cancer of among persons of Uzbek population. In National Research Center of Oncology, Tashkent/Uzbekistan 118 patients have been tested for HER-2 expression, and among 24 patients with stomach cancer was revealed HER-2-positive status of tumor. Among patients was prevalence of males: 66.9 % against 33.1 %. Middle age of patients was 57.3±0.8 years, an age range was from 29 till 80 years. The peak of disease was shown, that among all localizations affection of the upper part of stomach was prevailed – 41.5 %, middle part – 22.9 %, low part – 15.2 %, total affection – 20.4 %. Almost among half of patients were found adenocarcinoma of low degree of differentiation (49.2 %), moderately differentiated - among 15.3 %, high differentiated - among 17.8 % of patients. Mucous-plant-cellular cancer was found at 4.2 %. At 13.5 % of patients were found not differentiated forms of stomach cancer. Thus, it was revealed, that for the advanced stomach cancer of high differentiated forms are not characteristic. Thus, diffuse type of cancer was at 54 % and intestinal type at 46 % of patients. At 22 % of patients were found exophitic form of growth, at 31.3 % ulcerous-infiltrative and at 46.6 % diffuse-mucus form.

All the researched patients were divided into two groups: 1st group - 24 patients with hyperexpression of HER-2 had been made chemotherapy using regimen PLF: Cysplatlin 100 mg/m2, 1st day + 5-Flouracygli 1000 mg/m2, 1-3 days + Herceptin in doze 6 mg/kg once in 3 weeks (6 cycles). In control group in 26 patients it is lead only chemotherapy by the PLF regimen.
Leucovorin 100 mg/m², 1-3 days and Trastuzumab with dose of 6 mg/kg for 3 weeks (6 cycles). Criterion of administration of Trastuzumab is presence of cells in tumor with hyperexpression of HER-2, that is found by immuno-histochemical method. The preparation is administrated at expression 3+, and at its level 1+ or 2+ the additional analysis by method FISH is made. 2nd group - patients with negative expression of HER-2 had been made only chemotherapy using PLF regimen every 3 weeks without addition of Trastuzumab (6 cycles) (n=26). According all prognostic parameters both groups was identical.

RESULTS
According to studying results of immuno-histochemical parameters of patients with advanced stomach cancer of Uzbek population, hyperexpression of HER-2 receptor is met at 20% of patients (Figure 1).

Figure 1.Hyperexpression of HER-2 receptor.
HER-2 negative stomach cancer

HER-2 positive stomach cancer

These patients are mainly with stomach cancer of low differentiation, with infiltrative growth and with localization in upper part of stomach (Figure 2). In the main group the objective effect was noted in 54.5% of cases whereas in control group this parameter was 33.3%. At the moment of the analysis of preliminary data the median of duration of remission in compared groups has was 8.3 months, and 5.2 months. Additional criteria of efficiency were safety and quality of life. During research of special side effects with using of Trastuzumab had not been revealed.

CONCLUSION
At advanced stomach cancer with high level of HER-2 expression Trastuzumab increases frequency of objective effect and median of duration of remission.

All patients suffering from stomach cancer with low differentiation, infiltrative growth is recommended testing for HER-2.

In the long term it is necessary to study opportunities of using Trastuzumab in adjuvant treatment of operable stomach cancer.

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