

# Retrospective Analysis of Complex Treatment of Patients with the Rectum Cancer

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**Summary:** A total of 48 patients suffering from rectum cancer were included in this randomized study conducted at the Proctology Department of the Donetsk Regional Anti-Cancer Center. The 24 patients in group I were treated with Ukrain as monotherapy, 10 mg each second day before operation (up to a cumulative dose of 60 mg) and a total of 40 mg after surgical intervention. Repeated Ukrain courses (100 mg per course) were also given 6 months after surgical operation. Patients in group II (24 patients) received an intensive course of high fractional X-ray therapy (cumulative dose up to 25 Gr) with direct protracted endolymphatic chemotherapy with 5-fluorouracil (5-FU) instilled in 600 mg/m each day before operation, up to a cumulative dose of 5 g. In each case preoperative treatment was followed by routine surgical operation. 12-years survival in patients of the I group was as much as 75% (6 patients died), in patients of the II group – 45,8% (13 patients died). Comparative investigation of objective and subjective signs, analysis of results of instrument and X-ray data, as well as dynamic study of the histological structure of rectal tumors, indicate that Ukrain exerts a more potent malignotoxic and immunomodulating action than other types of anticancer treatment.

## Patients and methods

A total of 48 patients (30 men and 18 women) suffering from rectal cancer or who had been treated at the Proctology Department of the Donetsk Regional Anticancer Center were enlisted in a randomized study which was approved by the Ethics Commission of the Center. The patients ages ranged from 36-66 years, the mean value was 56.3 years. The experimental groups were made up of patients with rectal tumors corresponding to T3-4N0M0 and T3-4N1-3M0 stages of TNM classification without severe accompanying disease or complications of the basic process. Histological verification of tumors carried out in each case before starting the special treatment revealed adenocarcinomas at different degrees of differentiation in 89.7% of cases.

All patients were subdivided into two randomized groups. Group I comprised 24 patients who received monotherapy with Ukrain: i.v injections of 10 mg each second day before surgical operation (up to 60 mg cumulativ\* dose) and a total of 40 mg during the postoperative period. Additional repeated course; (100 mg Ukrain per course) were performed 6 months after surgical intervention. Patients in group II (n=24 received a preoperative intensive course of high-fractional X-ray therapy (5 Gr daily, up to 25 Gr) with direct endolymphatic chemotherapy with 5-FU (600 mg/m<sup>2</sup> daily), up to < cumulative dose of 5 g. After preoperative treatment all patients underwent a surgical operation. Only patients without verified distant metastases were included in the randomized study Metastatic invasion into regional lymphatic glands was found in 56.3% of cases (Table I) Where necessary, patients received corrective infusion, cardiotropic and genera reinforcement therapy.

The complex preoperative study involved the determination of tumor dimensions and mobility, general and biochemical analysis of the blood and urine, assessment of immune status (T- and B-lymphocytes count, concentrations of immunoglobulins A, M, G; plasms content of the circulating immune complexes (CIC) and phagocytic activity of neutrophils) In addition, the immune-enzymatic method was used to determine the blood content of a-feta protein (AFP) and carcino-embryonal antigen (CEA). Additional topographical data were obtained by means of abdominal sonography and computerized tomography. X-ray studies of the lungs and other examinations were also performed. Tumor dimensions, measured by rectoscopy, fibroscopy and irrigoscopy, varied from 2.8±3.4 cm to 8.6±9.8 cm.

## Results

After finishing the specific preoperative treatment for each group, repeated dynamic follow-up examinations were performed. These included assessment of patients general condition, expression of pain syndrome, and measurement of tumor dimensions. The toxicity of chemotherapy with reference to its influence on hemopoiesis was also determined for all groups of patients. The most expressed signs of the toxic action of chemotherapy were found in patients in group II who received combined endolymphatic chemotherapy and radiation therapy. The mean value of the Kamofsky Index decreased from 71.3 to 66.4. In contrast, practically no toxic effects were found in patients in group I, treated with Ukrain. Moreover, in these patients an improvement in the general condition and appetite was observed, as well as the disappearance of partial intestine impassability. Group I patients displayed a certain improvement in hemopoiesis with a statistically significant rise in erythrocyte and lymphocyte counts, while patients treated with combined endolymphatic chemotherapy and radiation therapy showed a tendency to develop anemia and lymphopenia. The Karnofsky Index increased to 78.3% from 70.8%. The most pronounced changes in immune status were also observed in group I patients who received Ukrain monotherapy (Table II). In this group a substantial rise in the T- and B-lymphocyte counts, increased phagocytic activity of neutrophils, and an increased content of immunoglobulins A, M, and G were observed. Reduced plasma concentration of AFP, CIC and CEA was characteristic for group I patients. No marked changes in immune status were detected in group I patients.

Reduced tumor dimensions were found in both groups of patients after preoperative therapy. Preoperative X-ray therapy in combination with endolymphatic 5-FU led to resorption of tumors in up to 18% of cases, while the mean value of tumor resorption with Ukrain monotherapy was 22%. Various kinds of rectal resection were performed following preoperative therapy. The majority of the surgical interventions (95.2%) were sphincter-saving in character and involved various kinds of abdominal-anal resections of the rectum. Two patients with tumors of the anal canal underwent resection according to Keny-Mylse. In total, postoperative complications developed in 9 (18.8%) cases. Postoperative complications were found to develop mainly in patients from group II - 7 cases (29.1%). In contrast, no postoperative purulent inflammatory complications were revealed in group I patients. Atony of the urinary bladder developed in 2 (8.3%) patients treated with Ukrain monotherapy.

**Clinical observation of all patient groups was conducted for a period of 12 years. 6 months after the first course of Ukrain monotherapy, all patients in group I were subjected to repeated Ukrain treatment with 10 mg i.v. every other day, up to a cumulative dose of 100 mg. In the course of observation of group II patients received complex chemotherapy and X-ray therapy. 12-years survival in patients of the I group was as much as 75% (6 patients died), in patients of the II group – 45,8% (13 patients died). In all cases prolongation morbi were revealed in patients who had metastasis in regional lymphatic nodes.**

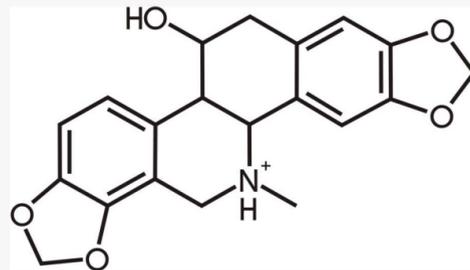


Table 1. Distribution of colorectal cancer patients according to TNM-classification.

TNM staging	5-FU+X-ray therapy	Patient groups
		<b>Ukrain therapy</b>
T3N0M0	2	1
T3N1M0	2	2
T3N2M0	1	1
T3N3M0	3	1
T4N0M0	8	10
T4N1M0	1	2
T4N2M0	3	2
T4N3M0	4	5
<b>Tcdal</b>	<b>24</b>	<b>24</b>

Table 2. Reported side effects in Ukrain monotherapy group.

Adverse event	Frequency of occurrence, # (%)	Severity Grade	Causality	Mean duration, hours	Treatment needed	Comments
Depression	3(13)	1-2	Possible	3-5	no	Mild or moderate mood alteration not interfering or sometimes causing difficulty performing some ADL
Insomnia	4(17)	1-2	Probable	2-8	no	Difficulty sleeping, not interfering or weakly interfering with ADL
Sleepiness / somnolence	1(4)	1-2	Probable	8-10	no	Somnolence or sedation interfering with function, but not interfering with ADL
General fatigue	6(25)	1-3	Possible	6-10	no	Mild, moderate, sometimes severe fatigue interfering with ADL
Increased fluid requirement	1(4)	1	Certain	1,5-2	no	lincrease in fluids intake, dry mouth sensation
Increased urination	1(4)	1	Certain	1,5-2	no	Mild increase in frequency and volume of urine, non affecting ADL
Local symptoms	10(42)	1	Possible	18-24-more	no	tension, tingling sensations, mild stabbing, burning and/or dragging pains, Itching, feeling of warmth in the tumor area not interfering with function and ADL
Nausea	3(13)	1	Possible	3-4	no	Short-lasting loss of appetite without alteration in eating habits
Fever	11(46)	1	Probable	2	no	38.0-39.0°C, not or slightly affecting ADL

Table 3. Parameters characterizing the immune status and hemopoiesis of patients

Parameters	5-FU + X-ray therapy		Ukrain therapy	
	before	after	before	after
Erythrocytes	3.9 ±0.35	3.4 ±0.21	3.9 ±0.36	4.11 ±0.24
Leukocytes	9.2 ± 0.96	7.4 ± 0.88	9.3 ± 1.21	9.1 ± 1.51
Lymphocytes	23.8±3.17	17.6 ±2.17	23.9 ±4.01	28.6 ±4.12
Rod-shaped	11.8 ±2.57	13.8 ±3.21	12.1 ±2.56	9.4 ± 8.87
Segmented	55.8 ±3.7	57.6 ± 2.96	55.3 ±3.61	53.4 ± 3.58
Eosinophils	3.5 ±1.11	2.8 ±0.93	3.2 ±0.84	4.3 ± 1.24
Monocytes	5.6 ±1.09	5.9 ±1.13	6.1 ±1.13	5.8 ±1.08
Proteins	71.02 ±2.18	67.4 ± 1.31	69.2 ± 2.03	76.1 ±2.67
Bilirubin	18.1 ±3.12	21.6±3.18	18.6 ±2.64	16.9 ±2.21
T-lymphocytes	38.8 ± 2.86	34.1 ±2.79	39.3 ± 3.26	46.2 ± 3.48
B-lymphocytes	9.12 ± 1.37	8.4 ±1.89	9.14 ± 1.36	11.2 ±2.71
Neutr. phag. activ.	80.2 ± 1.91	85.4 ±1.51	86.4 ± 2.02	98.1 ±2.1
CIC	279.2 ±17.6	296.1 ± 19.31	273.1 ± 18.1	211.6± 15.31
AFP	28.7 ± 2.81	30.1 ±3.03	26.2 ±2.01	5.1 ±0.84
CEA	4.8 ±1.02	4.5 ±0.87	4.8 ±0.91	1.2 ±0.18
MCA	16.2 ±1.83	18.4 ±2.12	17.8 ±1.93	4.1 ±0.76
igA	2.93 ± 0.86	3.14 ±0.56	2.87 ±1.17	4.12 ± 1.63
igM	0.76 ±0.11	0.86 ±0.18	0.72 ±0.12	0.96 ±0.21
gG	12.6 ±1.85	14.2 ±1.47	12.8 ±1.42	19.1 ±2.34

