Federal State Budgetary Educational Institution of Higher Professional Education "North Ossetian State Medical Academy" of the Ministry of Health of the Russian Federation

Guidelines

## "ONCOLOGY" IN CLINICAL RESIDENCE

Section 4. Basic principles of treatment of malignant neoplasms

Vladikavkaz 2023

Printed by decision of the Central Methodological Council of the North Ossetian Medical Academy of the Ministry of Health of the Russian Federation, Protocol No. .... from .. 201

Reviewers:

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Teaching sections of the discipline "oncology" in clinical residency: guidelines for teachers Associate Professor S.M. Kozyreva - Vladikavkaz: SOGMA, 2016. - 92p. head department, d.m.s. Associate Professor Khasigov A.V., Art. laboratory assistant Sautieva M.G.

Methodological recommendations are intended to help teachers of medical universities in organizing the educational process at the departments of oncology of postgraduate medical education. The recommendations are drawn up in accordance with the work program of the discipline "Oncology" of the main professional educational program of postgraduate professional education for students in residency in the specialty "Oncology". The recommendations provide for theoretical and practical forms of organizing training for clinical residents, the sequence of classes to systematize knowledge on the clinical course, diagnosis, treatment, and prevention of malignant neoplasms.

SOGMA, 2016 Compiled by: PhD associate professor Kozyreva S.M. head department, d.m.s. Associate Professor Khasigov A.V. Art. laboratory assistant Sautieva M.G.

TOPIC 4. "BASIC PRINCIPLES OF MALIGNANT NEOPLASMS TREATMENT"

1. Duration: 4 academic hours (1 academic hour - 45 minutes).

2. Venue: oncology dispensary.

3. The purpose of the lesson:

To comprehend the lecture material, to discuss in detail the possibilities of using surgical, radiation, medicinal, combined and complex methods in the treatment of malignant

neoplasms. To study the methods of treatment of oncological patients aimed at the radical elimination of the primary tumor focus and regional metastases, the prevention of the development of distant metastases, the restoration of disturbed homeostasis; draw up a treatment plan for a patient with a malignant neoplasm of one or another localization. To train residents in the basic principles of the treatment of malignant tumors, the choice of treatment methods at the stages of medical care, medical examination and preventive measures.

For this you need:

3.1. To systematize knowledge about the basic principles of the treatment of malignant neoplasms, about the methods used in the treatment.

3.2. To study the principles of surgical, combined and complex treatment of malignant neoplasms.

3.3. To train residents in conducting examinations and drawing up a treatment plan for patients with malignant tumors of different localizations.

3.4. The educational value of the topic: the analyzed material serves to develop the clinical skills of residents in drawing up a treatment plan for patients with malignant tumors of different localizations based on the use of the principles of surgical, combined and complex treatment of malignant neoplasms.

3.5. The origins of the topic: the residents acquired basic knowledge at the departments: normal and pathological anatomy, pathological physiology, histology and cytology, surgery, therapy.

3.6. Output of the topic: the knowledge and skills acquired in the classroom are necessary for mastering the principles of treatment of malignant different localizations.

Motivation of the theme of the lesson. Specificity of treatment of malignant neoplasms. The need to master the methodology for the correct preparation of a treatment plan for a patient with a malignant neoplasm, taking into account the extent of the spread of the malignant process based on the international classification of malignant neoplasms (TNM-classification).

Lesson plan.

1. Control test tasks.

2. Oral-speech survey on theoretical material (Principles of surgical, combined and complex treatment of malignant neoplasms. Principles and methods of radiation therapy of malignant tumors. Principles of drug therapy of oncological diseases. Palliative care.).

Test questions:

List the main methods of treatment in oncology Define combined and complex treatment in oncology List the tasks of neoadjuvant and adjuvant treatment in oncology What types of surgeries are performed on cancer patients? Name the principles of radicalism in oncology What is the principle of ablastic and antiblastic? What are the basic principles of radiation therapy What does tumor radiosensitization mean? List the types of ionizing radiation

What are the main goals of drug therapy for cancer patients

What is the difference between adjuvant and neoadjuvant chemotherapy?

What is the difference between systemic, regional and local chemotherapy? What tumors are treated with antiestrogens?

What effects on the tumor process does passive immunotherapy imply?

What is the difference between specific and nonspecific immunotherapy for cancer patients?

What is palliative care?

The difference between combined and complex treatment,

Who makes the treatment plan

How are treatment waivers handled?

At what localizations of cancer is combined treatment carried out,

What localizations of cancer are treated with microdose chemotherapy,

What is Targeted Therapy?

3. Listening and discussion of abstracts:

Surgical method in the treatment of cancer patients. The concept of ablastic and antiblastic, operability and resectability. Radical, palliative, cytoreductive, symptomatic operations. Radiation method in the treatment of patients with malignant neoplasms. Radiation therapy as an independent method of treatment, as a component of combined or complex treatment.

Radiosensitivity of tumor and normal cells. radio modifying agents. Types of ionizing radiation.

Drug therapy of malignant neoplasms. Chemotherapy. Hormone therapy. Immunotherapy.

4. Practical work of residents:

4.1. Drawing up a treatment plan for a patient with a malignant neoplasm of one or another localization (16 nosological forms).

Training in the methodology for the correct preparation of a treatment plan for a patient with a malignant neoplasm, taking into account the extent of the spread of the malignant process based on the international classification of malignant neoplasms (TNM-classification).

Mastering the methodology for the correct preparation of a treatment plan for a patient with a malignant neoplasm, taking into account the degree of spread of the malignant process based on the international classification of malignant neoplasms (TNM-classification).

4.2. Solution of situational problems.

FOUR BASIC TREATMENTS FOR TUMOR Surgical method Radiation therapy Chemotherapy Immunotherapy The main methods of special treatment in oncology are: surgery, radiation, chemotherapy. These methods can be used both separately and in various combinations. The choice of method and its effectiveness depends on the location of the tumor, histological structure, stage, general condition of the patient. In all cases, morphological verification of the neoplasm is mandatory, on the basis of which adequate treatment can be provided. In oncology, combined and complex methods are distinguished. Combined method of treatment is the use of surgery with radiation therapy in any sequence. Such a method will be complex when surgery or radiation therapy is complemented by chemotherapy. In addition to the three main methods, additional ones are used that increase the effectiveness of the main ones, or help reduce the negative effects on the body. These are immunotherapy, hormone therapy, local hyperthermia, etc. An important role in the treatment of cancer patients is played by symptomatic therapy, which consists in detoxification, adequate pain relief and treatment of disorders arising from tumor development.

Operations are characterized by aseptic, ablastic, antiblastic, sheathing, zoning. Operations can be performed using a scalpel, laser, ultrasound, cryodestruction and can be: reconstructive - restorative; · microsurgical; · plastic; · endoscopic, including laparoscopic; · savings. • Radical is an operation in which the tumor is removed within healthy tissues a single side with the surrounding tissue and regional lymph nodes. Palliative surgery is the removal of the primary tumor, leaving inoperable metastases. During such operations, for example, obstruction, bleeding are eliminated and prerequisites are created for possible radiation and drug treatment. Symptomatic operations include those in which some leading pathological syndrome that threatens life is eliminated. An example is gastrostomy surgery for inoperable esophageal cancer. Trial - these are surgical interventions when an operative access was performed, but the tumor could not be technically removed. Cytoreductive operations are performed to remove the main, sometimes significant, mass of the tumor. This is done, firstly, due to the impossibility of radical removal of the entire primary focus, and secondly, in order to create conditions for a more effective effect of chemotherapy drugs. Especially often, such operations are performed for ovarian cancer and its relapses, which are sensitive to chemotherapy and the higher the sensitivity, the smaller the mass of the tumor. Radical operations are now well developed for each localization and standardized. The standard operation, for example, for cancer of the right half of the colon, is a right-sided hemicolectomy. A radical operation can be combined if, along with the removal of the primary focus, an adjacent organ affected by metastases is removed or resected. For example, gastrectomy for gastric cancer with liver resection for metastases. A radical operation is considered extended if the generally accepted scope of lymphadenectomy is extended. For example, it is common for stomach cancer to remove the small and large omentums and the regional lymph nodes embedded in them. If this operation removes the para-aortic lymph nodes, along the hepatic artery, in the hepatoduodenal ligament, then such surgery will be considered extended. Asepsis is a prerequisite for successful outcomes of all operations, not only oncological ones. Ablasty is a method of operating, specific for surgery of malignant neoplasms, in which all tumor (blast) elements. N.N. Petrov wrote: "Cancer is entirely contained in cancer cells; to remove or burn them without residue means to cure the patient; to leave in place and disperse at least a minimal amount of living cancer cells over the wound means to do a bad job and often bring harm to the patient instead of good. The ablastic principle is implemented by a set of measures aimed at preventing tumor cells from entering the surgical wound and

hematogenous dissemination. It is necessary to adhere to careful tactics of surgical manipulations, do not crush or bite the tumor, but carefully remove it as a single block. Compliance with ablastics is facilitated by wrapping the surgical wound with sterile drapes with their replacement at certain stages of the intervention, along with frequent changes of gloves and instruments, performing thorough hemostasis, etc. Antiblastics is a set of measures aimed at destroying and removing tumor cells that could get into the surgical wound. For this purpose, the treatment of the latter with antiseptic solutions, for example, alcohol of 70% concentration, 3% hydrogen peroxide solution, is used. Operation within the anatomical fascial-fat pockets, as anatomical barriers that limit the spread of the tumor, helps to maximize the ablasticity and radicalism of the operation. The concept of "zoning" of surgical intervention is a surgical technique that takes into account the features of the spread of the primary focus (T) and suspected or detected tumor metastases to regional lymph nodes (N). In oncology, the concepts of operability and resectability are distinguished. Operable is a patient whose tumor is technically resectable, which depends on the stage of the process, and the functional state of a particular patient allows it to be removed. With unresectable tumors, due to the high prevalence, there are no technical possibilities for their removal. Modern oncological operations can be performed using ultrasound, scalpel, laser, cryodestruction. The rapid development of anesthesiology, resuscitation, medical technology, antibiotic therapy, transfusiology, as well as success in such areas as microsurgery, endosurgery, endoprosthesis, has led in recent years to the emergence of qualitatively more advanced methods of surgical treatment of cancer patients.

The crippling amputations and exarticulations were replaced by savings operations: reconstructive and restorative, microsurgical, plastic, endoscopic. New technologies help improve the quality of life, create conditions for faster and more complete rehabilitation of cancer patients. Radiation therapy Radiation therapy is currently one of the main and effective methods of treating malignant neoplasms and is used in combination with other methods or independently. Today there is a strong trend towards improving the results of treatment of cancer patients. There are currently more than 10 million survivors of the disease in Europe, 50% of whom have received radiation treatment. There is a trend towards a wider use of radiotherapy in various forms of cancer, which is associated with the development of organ-sparing treatment. This allows achieving high rates of physical and social rehabilitation of patients. Modern radiation therapy is a strictly scientific discipline based on fundamental physical and technical support, radiobiological substantiation and achievements of clinical and experimental oncology. Radiation therapy can be effective only if a number of conditions are met, relating not only to the correct supply of the required dose of radiation to the pathological focus, but also to minimizing radiation exposure to surrounding healthy organs and tissues, the correct choice of the type and energy of ionizing radiation, the most rational selection of the irradiation technique. Taking into account all the factors influencing the successful implementation of a course of radiation therapy is an extremely difficult task, which is solved in cooperation with specialists in radiology, medical physicists, mathematicians, biologists, and engineers. In radiation therapy, various types of ionizing radiation are used as an antitumor agent; when radiation is applied to biological objects, ionization occurs and a chain of radiation-chemical reactions occurs. In this case, one of the main roles is played by water radiolysis. The chain reaction ends with the release of free radicals, which are equally toxic to tumor and normal cells.

Radiation therapy is based on the ability of ionizing radiation to damage vital cell structures, primarily DNA, as a result of which these cells lose their ability to divide and die. There are lethal, sublethal and potentially lethal types of damage. In the range of energies and doses used in the clinic, sub- and potentially lethal injuries predominate. Their fate can be twofold - from full recovery to summation and transition to lethal. Normal tissues surrounding the tumor, primarily connective, can provide resorption (resorption) of dead tumor cells and replacement of the formed defect with a scar (reparation). For this reason, when using radiation therapy, they strive to selectively destroy tumor cells and preserve the normal tissues surrounding them. Under the influence of ionizing radiation, both in the tumor and in normal tissues, opposite processes develop - damage and recovery. The success of radiation therapy is possible only when damage processes predominate in the tumor, and recovery in the tissues surrounding it. The response of any tissue to exposure to ionizing radiation is determined by many factors, among which the main ones are the ability to repair (restoration of sub- and potentially lethal damage), repopulation, oxygenation and reoxygenation, and the phase of the cell life cycle at the time of their irradiation. The biological basis for the use of radiation therapy in oncology is the therapeutic interval, i.e. differences in the degree of damage and restoration of tumor and normal tissues at equal levels of doses absorbed by them. The longer the therapeutic interval, the easier it is to destroy tumor elements while maintaining the viability of surrounding tissues. The sensitivity of any malignant tumor to radiation depends on the specific features of its constituent cells and, first of all, on the radiosensitivity of the tissue from which the tumor originated. For the complete or partial destruction of malignant tumors, a sufficiently high dose of radiation is required. The dose, at the summing up of which one can count on the total destruction of the tumor, is called carcinocidal. On average, it reaches 60-80 Gy, although depending on the radiosensitivity of individual tumors, it varies widely from 30 to 100 Gy. The statement that malignant tumors should be divided into radiosensitive and radioresistant should be understood very conditionally. Due to heterogeneity, in the same neoplasm, there coexist areas that react differently to the effects of ionizing radiation. Due to the fact that a number of tumor characteristics are very dynamic and can change during the course of radiation therapy, it is very difficult to judge the initial radiosensitivity of each specific tumor. To carry out radiation treatment with guaranteed implementation of the planned irradiation plans, a whole complex of equipment is needed.

An important task is the choice of radiation energy, and the main factor in this choice is the depth characteristic of the dose distribution for photons and electrons of a given energy, which is necessary for tumors of various localizations. To create optimal conditions for remote irradiation, it should be possible to change the radiation energy depending on the depth of the pathological focus and the presence of critical normal organs adjacent to it. This can be ensured by the presence of accelerators generating bremsstrahlung in the range from 5 to 20 MeV, gamma therapeutic devices and X-ray therapeutic installations. Remote exposure can be static and mobile. Static exposure is produced through one or more input fields and is called single-field or multi-field, respectively. Multifield allows you to reduce the dose in superficial tissues. During mobile irradiation, the source moves around the patient, while remaining "pointed" at the pathological focus. Three methods of mobile irradiation are most common: rotational (the source moves in a circle with the center in the target and is used for deep-seated tumors), sector (the source moves along an arc within the selected angle), tangent-eccentric (the beam is directed tangentially to the patient's body, passing under its surface at a shallow depth and is used for superficially located

tumors of great extent). When using contact methods of irradiation, radioactive sources are placed in tumors or in close proximity to it. Full implementation of the energy of the emitters at a distance of up to several mm makes it possible to create high doses of radiation in the target organ without damaging the surrounding tissues. There are other types of radiation therapy: proton therapy, neutron therapy, heavy ion therapy, negative pion therapy. From the point of view of the antitumor effect, a single dose equivalent to a carcinocidal dose is preferable, but there is a risk of irreversible damage to normal tissues. Therefore, in order to spare normal tissues, the total dose is divided into parts; they are fractionated and irradiated at different intervals. When choosing a strategy for temporal dose distribution in radiation therapy, at least two main factors should be taken into account: the biological parameters underlying it and the specific temporal distribution of the dose in the irradiated volume. To search for a rational irradiation scheme, general biological laws are used, based on the qualitative and quantitative characteristics of the reactions of various tissues to the action of ionizing radiation, taking into account specific clinical situations, which are determined by the general condition of the patient, the degree of prevalence and type of malignant tumor.

The main requirement of clinical radiology is to create the maximum dose in the pathological focus with minimal exposure of normal tissues. This principle can be implemented by choosing the optimal options for the spatial distribution of radiation energy (dosimetric planning). Due to the presence of various sources of radiation, a variety of methods and methods of irradiation, a sufficient set of special devices and devices forming a radiation beam, it is possible to irradiate a volume of any configuration. Forming the optimal spatial distribution of the radiation dose by physical methods, various methods of radiomodification are simultaneously used, which provide selective protection of normal tissues or increase the degree of damage to a malignant tumor, i.e. expand the therapeutic interval. All modern methods of radiomodification are based on the achievements of radiobiology. The revealed dependence of the degree of radiation damage to tissues on their oxygen saturation (i.e., the oxygen effect) formed the basis for the use of hyperbaric oxygenation and electroacceptor compounds as tumor radiosensitizers, and tourniquet and general gas hypoxia as protectors to protect normal tissues. Some anticancer drugs are also used for radiosensitization. Universal sensitizers include hyperthermia, which increases the degree of oxygenation due to increased blood flow and inhibits the processes of postradiation recovery. For the same purpose, hyperglycemia is used. Variants of polyradiomodification are known. When using radiation therapy as an independent method, depending on the specific situation, which is determined by the characteristics of the malignant disease and the general condition of the patient, there are radical, palliative and symptomatic treatment. Radical radiation therapy is used to completely destroy the tumor parenchyma, resorption of the tumor and its regional metastases, with the expectation of curing the patient. Radical radiation therapy includes irradiation of the primary focus and areas of regional metastasis. Applied doses 60-80 Gy. The tasks of palliative radiotherapy include inhibition of tumor growth and reduction of its volume, due to which it is possible not only to prolong the life of patients, but also to improve their general condition (quality of life). In these cases, doses of 40-50 Gy are used. Symptomatic radiation therapy can help eliminate severe symptoms of a malignant process and improve the quality of life. Special

short courses of radiation therapy have been developed to quickly relieve severe symptoms. One of the main conditions for the success of radiotherapy is a carefully designed radiation plan, including the definition irradiation volume, target localization, level of absorbed doses (in tumor and normal tissues). Radiation therapy planning includes clinical topometry, dosimetry and follow-up monitoring of the planned plan from session to session.

It has been established that the deviation of the focal dose from the planned one in the direction of its increase by 5% leads to clinical manifestations of the reactions of normal tissues, as well as the deviation in the direction of decrease - to an increase in the number of relapses. Like other treatments, radiation therapy can be accompanied by reactions and complications. The main factors on which they depend are single and total doses, the amount of exposure, the individual characteristics of the body, the state of the tissues in the amount of exposure. During the entire course of radiation therapy, it is necessary to systematically monitor the patient's condition, the rate and degree of tumor regression, the development of general and local reactions and complications. With adequate planning, general reactions are mild and disappear quickly after completion of radiation therapy. Only when irradiating large volumes, especially in the pelvic region, abdominal and chest cavities and summing up relatively high total doses, nausea, vomiting, headaches, and a change in the picture of peripheral blood can be observed. Methods for their correction have been developed. The emergence of a fundamentally new modern radiation therapy, which replaced the past, purely empirical, allows us to recognize this method as a highly effective scientifically based method of antitumor effects. Principles of chemotherapy The term chemotherapy in oncology refers to the treatment of malignant neoplasms with the help of cytostatics, that is, drugs that selectively inhibit the proliferation of tumor cells or irreversibly damage them. In modern oncology, along with cytostatics, hormonal agents and biological preparations are widely used, therefore, the essence of the method more accurately reflects the concept of drug therapy for malignant tumors.

In a broad sense, the term chemotherapy can be used as a synonym for drug therapy and reflect the full variety of options for drug therapy of neoplasms. Being, along with surgery and radiation therapy, the main method of treatment, chemotherapy, unlike local methods, provides an integrated approach, affecting tumor cells scattered or circulating in the body, which are so characteristic of most malignant neoplasms. The development of cancer drug therapy began with the accidental discovery of the lymphotoxic effect of mustard gases used during World Wars 1 and 2. An analogue of a chemical warfare agent, nitrogen mustard, became the first cytostatic agent successfully used to treat various types of lymphomas in the forties of the last century. The first experience of chemotherapy was published in 1946, since then chemotherapy has firmly entered the practice of treating malignant neoplasms, eventually becoming the leading and most rapidly developing method of treatment in oncology. Currently, the effective use of antitumor drug therapy requires a deep understanding of the process of cell growth and death, the fundamentals of pharmacodynamics and pharmacokinetics of drugs, and their mechanisms of action. Advances in molecular biology have become an impetus for understanding the pathways of intracellular signal transduction and cell cycle regulation, thanks to which we have witnessed the creation and appearance in clinical practice of drugs with targeted action the so-called "target" drugs. The main properties of malignant neoplasms. Unlike cells of healthy organs and tissues, malignant ones have a number of features. The main properties

of malignant neoplasms that ensure the steady progression of the disease leading to the death of the organism are the following: clonality: the tumor arises from a single stem cell that proliferates with the formation of clones. 32 Autonomy: Growth is not regulated by the body's normal physical and chemical influences. Anaplasia: loss of normal cell differentiation. Invasive growth and metastasis: cells acquire the ability to unrestricted growth and dissemination to other organs and tissues. A malignant tumor can metastasize with the flow of lymph and blood even with a microscopic size of the primary focus, with an increase in the size of the tumor, the likelihood of metastasis also increases. Under these conditions, carrying out only local methods of treatment (surgery, radiation therapy) does not lead to a cure. The use of chemotherapy allows for the prevention of metastasis at local stages, and has a therapeutic effect in the presence of clinically detectable metastases, becoming the main method of antitumor treatment in conditions of dissemination. Objectives of chemotherapy: The main objectives of treatment in oncology, including chemotherapy, is to cure the patient, which means the absence of signs of the disease, longterm relapse-free survival with a satisfactory quality of life. About 50% of cancer patients are curable. If a cure is not possible, the main tasks are to increase the life expectancy of patients and eliminate the symptoms caused by the presence of a tumor. There are curative, adjuvant and neoadjuvant chemotherapy. In cases where chemotherapy is the main independent method of treatment aimed at achieving remission and increasing the patient's life expectancy, it is called therapeutic. Adjuvant chemotherapy implies its appointment after an operation or radiation therapy according to a radical program, in which case the primary focus is cured and the effect is aimed at suppressing subclinical micrometastases, therefore it is also called prophylactic. Significant disadvantages of chemotherapy after local treatment are: 1. the inability to determine the individual the sensitivity of the tumor to ongoing drug treatment 2. the time of the start of systemic treatment is delayed, during which distant metastases can be realized. This gave impetus to the development of neoadjuvant chemotherapy, when drug treatment is prescribed as the first stage after diagnosis, before surgery or radical radiation therapy. This reduces the biological activity of the tumor, reduces its size, increases resectability, and in some cases reduces the amount of surgery and conduct organ-preserving treatment. At the same time, it is possible to determine the individual sensitivity of the tumor to ongoing chemotherapy based on an objective assessment and determination of the degree of therapeutic pathomorphosis, which is established during the histological examination of the removed tumor after surgery. The pronounced degree of tumor damage is an indication for the continuation of chemotherapy according to the same scheme as before the operation. Conversely, in the case of a low degree of pathomorphosis, the issue of changing the treatment program is considered. Efficiency mark. To objectify the assessment of the effectiveness of chemotherapy, special criteria have been developed. Currently, 2 systems are mainly used: RECIST - proposed by the US National Cancer Institute and WHO criteria.

WHO Criteria for Evaluating the Efficacy of Chemotherapy Complete remission (complete regression) - the absence of all signs of the tumor Partial remission (more than 50% tumor reduction) Stabilization (less than 50% decrease or no more than 25% increase) Progression (greater than 25% increase or appearance of new lesions) In addition, there are time criteria for evaluating the effectiveness of therapy: 2. Overall survival - the percentage of patients who are alive at the time of analysis 3. Median time to progression - the average time from the start of treatment to progression for the study population of patients 4. Median survival - time from start treatment until half of the patients included in the study are still alive. In the case of adjuvant (prophylactic) chemotherapy, the evaluation of effectiveness is possible only according to temporary criteria.

Arsenal of Chemotherapy Means Currently used antitumor drugs belong to the following pharmacological groups: alkylating agents, antimetabolites, antitumor antibiotics, herbal preparations, enzyme preparations, hormones, biological response modifiers and targeted agents. One of the most numerous groups of anticancer drugs is alkylating agents (Table 8), the main mechanism of action of which is the alkylation reaction, the substitution of a hydrogen atom in organic compounds for an alkyl group; DNA damage is the determining factor in cell death.

## Alkylating agents

1 Chloroethylamines Embihin (Mustargen, Caryolysin), Chlorambucil, Melphalan, Sarcolysin, Dopan, Cyclophosphamide, Ifosfamide, Myelobromol, Prospidin, Temodal

2Aziridines (ethyleneimines) Thiophosfamide, Hexamethylmelamine (Hexalen), Fluorobenzotef, Imiphos, Fotrin

3Esters of disulfonic acids Myelosan

4Nitrosourea derivatives BCNU (Carmustine), CCNU (Lomustine, Belyustin), ACNU (Nidran), Aranose, Mustophoran, Streptozotocin, Nitrulline

5Methylating agents (triazines) Dacarbazine (DTIK), Procarbazine (Natulan)

6Complex compounds of platinum Cisplatin, Carboplatin, Cycloplatam, Oxaliplatin (Eloxatin)

The group of antimetabolites is characterized by similarity with natural metabolites necessary for the synthesis of nucleic acids, being included in the exchange of a tumor cell instead of a natural metabolite, they lead to cell death due to impaired enzyme functions. For the first time, the stimulating effect of folic acid on leukemic cell cultures was described by Sidney Farber in 1946; this served as the basis for the development and introduction into clinical practice of the first subgroup of antimetabolites - folic acid agonists (antifolates).

## Antimetabolites

Folic acid antagonists (antifolates) Methotrexate, Trimetrexate, Pemetrexed (Alimta)
Pyrimidine Antagonists 5-Fluorouracil, Flutorafur (Tegafur), UFT, Azacitidine, Capcitabine (Xeloda), Cytarabine (Cytozar, Alexan), Gemcitabine (Gemzar)

3. Thymidylate synthetase inhibitors Tomudex

4. Purine antagonists 6-Mercaptopurine (Purenetol), 6-Thioguanine (Lanvis), Pentostatin, Cladribine, Fludarabine (Flyudara)

5. Ribonucleoside reductase inhibitors Hydroxyurea (Hydrea)

Among the preparations of natural origin (Table 10), antitumor antibiotics, enzymes and substances of plant origin are distinguished.

Anticancer drugs of natural origin

1. Actinomycins Dactinomycin (Actinomycin D)

2. Anthracyclines Daunorubicin (Daunomycin, Rubomycin, Doxorubicin (Adriamycin,

Adriablastin, 36 Doxolem), Epirubicin (Farmorubicin), Carminomycin, Aklarubicin, Idarubicin (Zavedos)

3. Anthracenidiones Mitoxantrone (Novantron)

4. Phleomycins Bleomycin, Bleomycetin, Peplomycin

5. Derivatives of aureolic acid Olivomycin, Mithramycin

6. Other antibiotics Bruneomycin, Mitomycin C (Mutamycin) Herbal products

1. Mitosis inhibitors Vinca alkaloids Vinblastine, Vincristine (Onkovin), Vindesine,

Vinorelbine (Navelbin) Taxanes Paclitaxel (Taxol, Intaxel), Docetaxel (Taxotere)

2. DNA topoisomerase inhibitors Topoisomerase inhibitors

I Topotecan (Hycamtin), Irinotecan (Campto), Camptothecin Topoisomerase inhibitors

II Podophyllotoxins - Etoposide (Vepezid), Teniposide (Vumon)

V. Enzyme preparations L - asparaginase; PEG - asparaginase (Oncaspar)

Biotherapy of malignant tumors

Interferons

1. Cytokine therapy Interleukins· Colony-stimulating factors· Non-conjugated·

2. Monoclonal antibodies Conjugated · Anti-idopathic (vaccines)

3. Vaccine therapy 1. Autologous 2. Allogeneic 3. Genetically modified Direct inhibitors of neoangiogenesis (MABs to

4. Anti-angiogenic therapy VEGF ) Indirect inhibitors of neoangigenesis  $\cdot$  (decrease in synthesis of GF ) Inhibitors of matrix metalloproteinases  $\cdot$  Retinoids

5Differentiating agents Antisense therapy (antisense RNA synthesis)

6. Gene therapy Replacing a damaged gene