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БИОЭТИЧЕСКИЕ ПРОБЛЕМЫ, СВЯЗАННЫЕ С РАЗВИТИЕМ И ИСПОЛЬЗОВАНИЕМ ТЕРАПИИ Т-КЛЕТКАМИ С ХИМЕРНЫМ АНТИГЕННЫМ РЕЦЕПТОРОМ ПРИ РАКЕ КРОВИ

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BIOETHICAL PROBLEMS ASSOCIATED WITH THE DEVELOPMENT AND USE OF CHIMERIC ANTIGEN RECEPTOR T-CELL (CAR T-CELL) THERAPY IN CASE OF BLOOD CANCERS

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Резюме: В статье рассмотрены биоэтические проблемы, связанные с развитием и использованием терапии Т-клетками с химерным антигенным рецептором при раке крови; описаны возможные осложнения, рациональность и эффективность использования этой терапии в лечении различных видов рака. Авторы предлагают данное исследование, проведенное среди 148 студентов и преподавателей БГМУ с целью выяснить связано ли внедрение новых методов лечения с какими-либо биоэтическими проблемами.

Ключевые слова: методы лечения рака, терапия Т-клетками с химерным антигенным рецептором, принцип безопасности, принцип дискриминации, принцип автономии.

Resume. The article considers emerging bioethical problems associated with the development and use of CAR-T Cell therapy in case of blood cancers, describes the possible complications, rationality and effectiveness of the use of this therapy in the treatment of different types of cancer. The authors provide the results of the survey carried out among 148 students and teachers of BSMU to find out concerning bioethical problems associated with implementation of novel treatment techniques.

Keywords: cancer treatment methods, Chimeric Antigen Receptor T-Cell therapy, the principle of safety, the principle of discrimination, the principle of autonomy.

Relevance. Malignant neoplasms are currently one of the most common causes of death in the world. The effectiveness of isolated use of some traditional treatments for malignant tumours, such as surgery, chemotherapy and radiotherapy, has certain limitations. Therefore, development of new methods of preventing malignant neoplasms based on modern molecular biology and genetics is particularly relevant, one of them being Chimeric Antigen Receptor T-Cell (CAR T-Cell) therapy. This immunotherapy consists of using modified T-cells called chimeric antigen receptor T-cells to recognize and kill cancer cells. It is known that CAR T-Cell therapy can be effective in various types of cancer and it enables physicians and patients to succeed in fighting against haematological malignant tumors. However, implementation of new treatment methods is accompanied by some side effects and bioethical problems.

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Aim: to consider the possible complications and main ethical problems of the use of CAR T-Cell therapy in the treatment of different types of cancer as well as to substantiate the rationality and effectiveness of its use.

Objectives:

1. To substantiate the effectiveness of CAR T-Cell therapy in the treatment of different types of cancer.
2. To consider the main ethical problems of the use of CAR T-Cell therapy.
3. To reveal the opinions of teachers and students of Belarusian State Medical University about the presence of bioethical problems in the use of novel treatment techniques, including CAR T-Cell therapy.

Materials and methods. An overview of scientific literature including books, articles devoted to new methods of cancer treatment were analyzed and summarized. A survey of 148 respondents from Belarusian State Medical University was conducted to reveal their opinion about the presence of bioethical problems in the use of novel treatment techniques, including CAR T-Cell therapy.

Results and their discussion. Malignant neoplasms are currently one of the most common causes of death in the world. For decades, the basic cancer methods have been surgery, chemotherapy and radiation therapy.

In addition to the traditional cancer treatments, the development of new methods of preventing malignant neoplasms based on modern molecular biology and genetics is being carried on.

A recently developed cancer treatment technique is Chimeric Antigen Receptor T-Cell (CAR T-Cell) therapy. It consists of using modified T-cells called chimeric antigen receptor T-cells (CAR T-cells) to recognize and kill cancer cells. [1]

CAR T-cells are receptor proteins that have been engineered to give T-cells the new ability to target a specific antigen. The chimeric receptors have properties of both antigen-binding and T-cell activating functions. CAR T-Cell therapy has been successfully used in the treatment of patients with various types of blood cancer (lymphomas, some forms of leukemia, multiple myeloma).

Chimeric Antigen Receptor T-Cell therapy is divided into five steps: T-cell collection, cell engineering, growing T-cells, chemotherapy, infusing T-cells. Recovery is expected to occur within two or three months.

CAR T-cell therapy:

• boosts the immune system;

• improves immunogenic memory, which allows treating local and distant metastatic lesions;

• recognizes and eliminates damaged cells and cells infected with harmful pathogens, such as viruses and cancerous cells;

• reduces the need for aggressive chemotherapy;

• may prevent or cure cancer relapse after transplant surgeries.

However, the use of CAR T-cell therapy is associated a risk of side effects, primarily hypercytokinemia and non-specific cytotoxicity. They can lead to multiorgan deficiency syndrome and result in death. [2]

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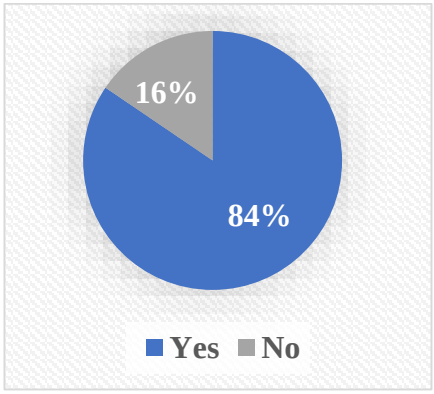
Besides, the use of any novel therapy is accompanied by certain ethical problems that can slow down its implementation.

To reveal the opinions of teachers and students of Belarusian State Medical University about the presence of bioethical problems in the use of novel treatment techniques, including CAR T-Cell therapy, a survey of 148 BSMU teachers and students aged 17-50 was conducted.

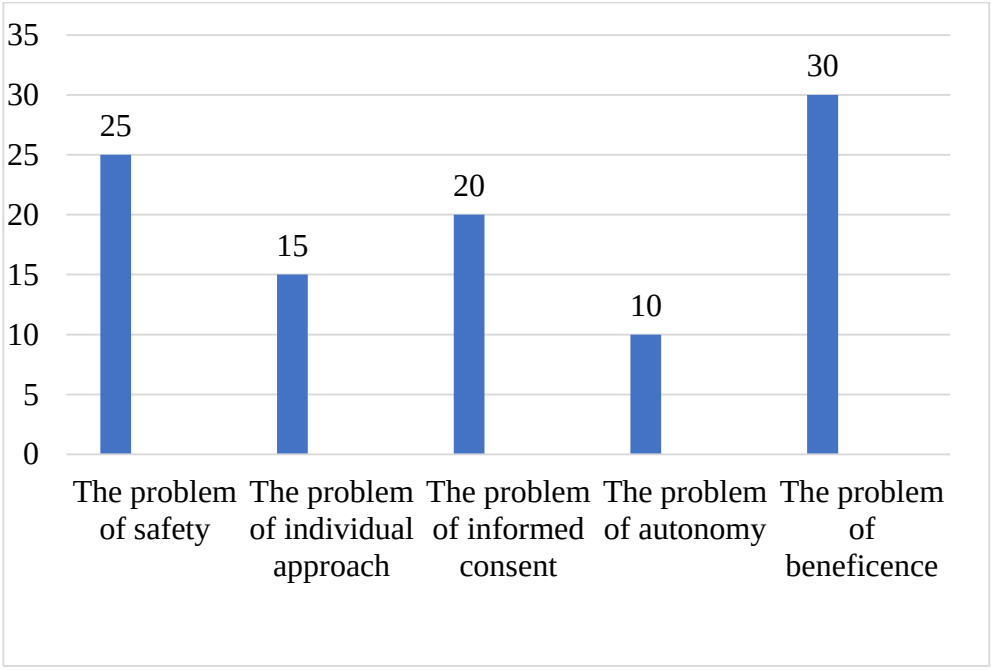
The respondents were offered a questionnaire, which included the following questions:

1. Do you think the development of new methods of cancer treatment is accompanied by any bioethical problems?

2. If yes, what problems can it be associated with?



Diag. 1 – Respondents' attitude to the bioethical problems, associated with the development of new methods of cancer treatment



Diag. 2 – Bioethical problems, accompanying the development of new methods of cancer treatment

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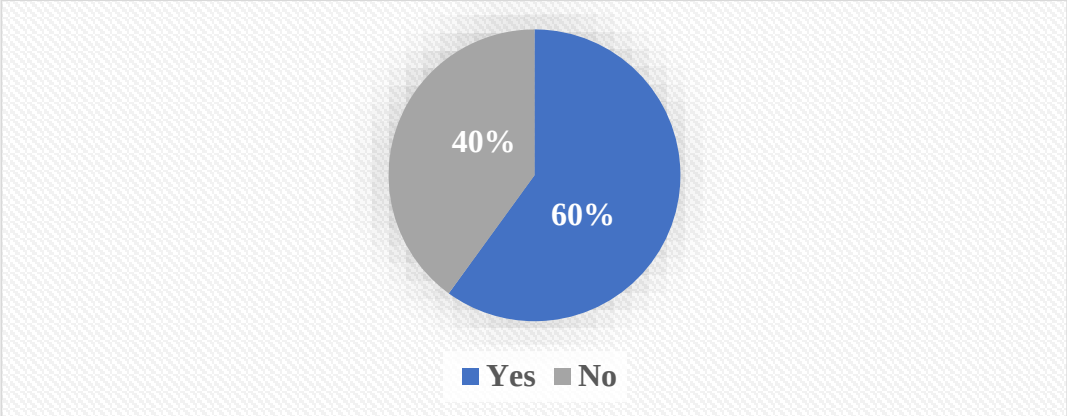
The survey carried has shown that 125 respondents (84,5%) consider the development of new methods of cancer treatment to be certainly accompanied by some bioethical problems, for example, the issues of safety, individual approach, informed consent, autonomy and beneficence. (Diagr. 1, 2).

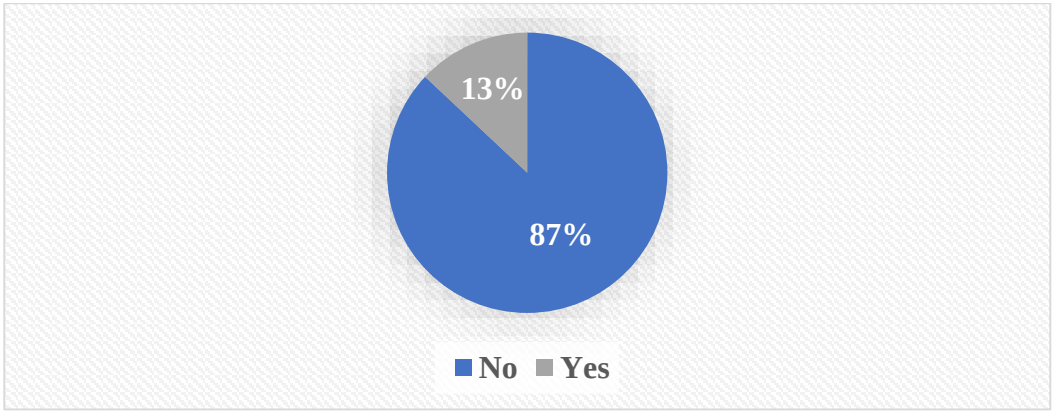
3. Would you like to try a novel method of treatment being tested? Please, explain why.



Diag. 3 – Respondents' attitude to a chance of participation in a trial of a novel treatment method

89 respondents (60%) stated they would sign an informed consent for a new method of treatment being tested in case of necessity, because they believed that in this case people should take all the opportunities to survive. 59 respondents (40%) noted that they wouldn't like to take part in testing novel methods of treatment, because they thought they might live longer without approved methods of treatment (Diagr. 3).

4. Would you give an informed consent for your family member to receive a novel drug? Please, explain why.



Diag. 4 – Respondents' attitude to a chance of relatives' participation in a trial of a novel treatment method

129 respondents (87%) considered that in case of necessity they wouldn't give an informed consent for their family members to receive a novel drug, because they didn't want to endanger the relatives and be responsible for their death. However, 19 of the interviewed people (13%) responded they would sign the informed consent and explained that in case of

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cancer they would take all the opportunities to help their family members to survive. (Diagr. 4).

From our point of view, the problem of safety plays the main role because of the risk of life-threatening side effects of the therapy on human health. The patient's safety can also be guaranteed in case of observing the principles of:

• Non-maleficence - the human biomedical research cannot be considered legal if the importance of research is disproportionate to the risk to humans;

• Benificence – the interests of the participant of the experiment are always more important than the interests of science and society;

• Autonomy – research on human being is always voluntary and the participant has the right to refuse from participation in the research at any time;

• Informed consent – the research is carried out only with the written consent of the participant or his legal representative. Each potential participant in the experiment should be informed of its aims, methods, expected outcomes and potential hazards, as well as of the rights and guarantees of the participant;

• Justice – participants must be provided with adequate and understandable information supported by documents. All new research information related to the project participation should be given to patients within a reasonable time;

• Human dignity – any personal information obtained in the course of biomedical research is considered to be a matter of medical confidentiality. [3]

Conclusions: the development of new methods of treatment is always associated with emergence of bioethical problems which should be carefully considered to prevent both physical and psychological harm to the patient. Experiments on humans should be carried out only if there are no alternative efficiency comparable methods of research. Strict laws should be developed regarding privacy and confidentiality of the patient's data and informed consent for the treatment.

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