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MODERN LANDSCAPE OF INNOVATIVE TECHNOLOGIES IN OPTIMIZING THE QUALITY OF LIFE OF CANCER PATIENTS

In the era of the intensive development of post-genomic technologies, it is reasonable to review the modern strategy for solving the problems of cancer patients. The current trend of the new paradigm is based on the knowledge and possibilities of correcting molecular genetic processes based on the principles of precision medicine. The key role in implementing such an approach belongs to modern innovative technologies, among which omics technologies occupy a special place. The genesis of the symbiosis of medical-biological and cybernetic technologies aimed at processing information databases becomes the subject of learning the functioning of complex biological systems. Today, for the dynamic development of the implementation of precision medicine based on innovative technologies, it is worth concentrating the efforts on the deep consolidation of transdisciplinary approaches that can form an algorithm of a new market of medical services aimed at improving the quality of life.

Keywords: quality of life, precision medicine, innovative technologies, cancer patients.

In the era of the intensive development of post-genomic technologies, bitter statistics about the steady rise of cancer incidence dictates the need to review the modern strategy in overcoming the challenges of one of the most complex medical and biological problems of our time. According to the WHO, in the near future, there are no grounds for optimism regarding cancer morbidity, while cancer mortality is increasing significantly [1].

In Ukraine, against the background of the ongoing war, this problem will be even more difficult. The risks of cancer growth will increase not only due to a significant local pollution of the environment with carcinogenic compounds resulted from numerous explosions and fires (eco-genocidal factors) but also to the distress of wartime, which affect mental and physical health triggering the mechanisms that induce the development of pathological processes. Right now, cancer is rapidly gaining a new momentum and is becoming a disease not only of the elderly. Presently, it is detected in much younger people, and the aggressiveness of its course is increasing [2—4].

The unwavering desire of the global community of oncologists to limit the development of the negative consequences of cancer is particularly clearly reflected in the chronological order, in the period

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of the last half-century. In the 70s of the XX century, great hopes were placed on a quick solution to the problems of cancer after the discovery of the functions of oncogenes, for which the authors of these studies, D. Baltimore, R. Dulbecco and H. Temin, were awarded the Nobel Prize in 1975. An ambitious task was set by the highest stands of the Congresses and Conferences — to curb this disease by 2000. However, despite the intensive research and the significant efforts of scientists and doctors, it turned out that this goal was unattainable for the specified term. Later, in 2003, the announcement about the decoding of the genome again gave the grounds for optimism. Although this event deepened the understanding of the individual mechanisms of carcinogenesis, it did not lead to a revolutionary breakthrough in the timely diagnosis and treatment of cancer. A similar situation arose after the completion of other meta-projects devoted to the identification of the human oncogenome and microbiome. While we understood much deeper the nature of this extremely complex pathological process, even these discoveries did not put specialists much closer to the victory in their fight against cancer [5—8].

A series of "disappointments" in the rapid victory over cancer and the emergence of new clinical problems, such as drug resistance, contributed to the rethinking and revision of the existing anticancer strategies. It is worth noting that at the beginning of the XXI century, in wide circles of specialists, it became clear that the defeat of cancer is a very far-fetched goal and requires a conceptual revision of the existing priorities. In return, instead of striving to finally overcome the disease, the concept of switching the malignant process into the chronic form and concentrating efforts on improving the quality of life (QoL) of patients began to sound more and more common.

Indeed, QoL is a multifactorial economic-philosophical category that constantly evolves and characterizes the material and spiritual comfort of people's existence. At the same time, one of the key units of its measurement is the medico-biological term — life expectancy. It is therefore considered that QoL is a measure that should account for the duration of life. QoL encompasses all one's sensations from pleasure to suffering as well as the influence of environmental factors [9].

An assessment of the QoL of cancer patients at different stages of their treatment, when physical, mental, and social health falls into a zone of special turbulence, requires special understanding. In this case, several additional parameters are introduced to assess the patient's QoL, which greatly complicates its characterization [10—12].

Today, there are quite a lot of models that allow assessing the QoL of patients, including the well-known models of the WHO, Karnavskyi, Wilson and Cleary, Deikers, *etc.* [13]. These models cover a wide range of patients' problems, including their age, gender, disease symptoms, environment, work, education, home, society, social factors, finances, treatment, *etc.* This indicates that each of the mentioned factors can significantly affect the patient's QoL. Neglecting a factor or their sum can significantly affect both the patients' survival and life expectancy, and most importantly their QoL.

We have analyzed the dynamics of the number of scientific publications in the PubMed databases related to the measurement of QoL. Over the past 2—3 years, the dynamics of the level of global publications regarding the general characteristics of QoL has been gradually increasing, becoming more and more relevant each year. However, when our attention was paid to the number and dynamics of the scientific publications regarding the QoL of cancer patients, the general picture turned out to be depressing (Fig. 1). Thus, in particular, according to Rizzo et al. [14], in 2021, the assessment of QoL in numerous clinical studies was partially or completely absent and not discussed in 72.2% of cases.

That is why many non-rhetorical questions arise regarding the assessment of QoL, which can influence a change in the priority indicator in the fight against the challenges caused by cancer:

1. Is it possible in the emerging era of the paradigm of modern medicine based on precision principles, to underestimate the role or ignore the QoL as one of the key indicators of the effectiveness of providing specialized medical care?

2. Are there modern tools that can be effectively used in the formation of a multidisciplinary model of QoL?

3. Is humanity able to bring the dream of overcoming cancer problems closer?

It is important to note that, on the one hand, the basis of the modern trend of the new paradigm

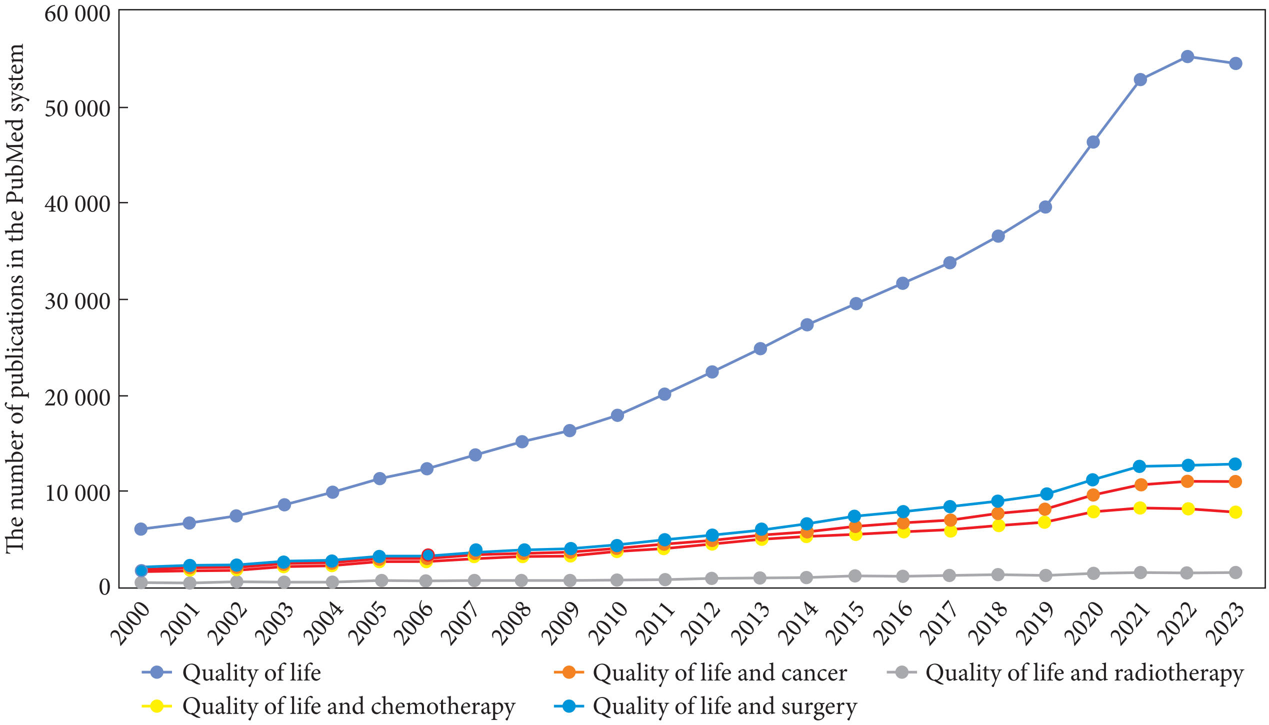

Fig. 1. Scientific publications in PubMed databases by search queries

is knowledge and the possibility of correcting molecular genetic processes in a specific person, and on the other hand, the modern structure of the world economy sees in each individual a bearer of the budget-forming process — profit. The coincidence of the interest in the involvement of the opportunities of medicine and the economy raises the importance of QoL indicators to a new level.

The key role in the implementation of such an approach belongs to modern innovative technologies. Among them, omics technologies occupy a special place, as far as they can provide unique indicators and analyze the course of molecular genetic processes at different levels of systemic biology [15, 16].

Until recently, QoL parameters were measured based on the medical history data, general clinical examinations, risk factors, radiography, etc., but today there is an opportunity to use a colossal arsenal of the standardized parameters obtained based on functional genomics, epigenomics, transcriptomics, interferomics, proteomics, metabolomics, glycomics, lipidomics, etc., which allow characterizing the structure of individual proteins, their binding sites, initiation and transduction of signal cascades, etc. The arsenal of existing innovative technologies, as a key tool for registering the functions of complex hierarchical systems of deep processing and data analysis, is the basis of the algorithm for the implementation of precision medicine [17, 18].

The definition of the term "precision" or "personalized" medicine defines this approach to the prevention, diagnosis, and treatment of the patient as a revolutionary leap based on scientific knowledge about the course of molecular biological processes.

Our contemporaries often claim that the introduction of this term into the field of medical activity refers to the transitional period between the XX and XXI centuries, when in 1998 the first monograph "Personalized Medicine" by K.K. Jain was published [19]. However, for the sake of objectivity, it is worth mentioning the most famous doctor of Antiquity — Hippocrates, who always put the person, not the disease, at the center of the art of treatment.

This approach allows for a much broader understanding of the nature of the malignant process, identification of new markers, as well as the potential targets of the drug effects. The identification of the mutations, translocations, hypo- or hyperexpression of individual genes forms a unique molecular profile of the tumor lesion.

The changes in the gene expression are largely due to the impairment of the program of their epigenetic regulation via the changes in the DNA methylation status, which is accompanied by both hypomethylation of the genome as a whole and hypermethylation of promoters of individual genes [20]. A modification of gene expression is not only one of the causes of malignant transformation of cells but also a factor affecting invasion, metastasis, and response to chemotherapy. To date, it has been proven that the variability of these processes affects the formation of the extracellular matrix, the structure of the stromal component of tumors, vascularization, the number and types of cells of the immune system, microenvironment factors, and metabolic features, which can simultaneously restrain and provoke cancer progression [21—24]. The rapid progress in the study of the mechanisms of epigenetic regulation has made it possible to identify the unique regulatory capabilities of microRNAs. It has been proven that these small non-coding RNA molecules affect the proliferative activity of cells, their differentiation, the processes of signal transduction, the apoptotic program, and even orchestrate the relationship between the tumor and the organism [25—27].

The individual variability of the processes in the tumor microenvironment and the activity of the metabolic processes in the body as a whole can significantly affect the effectiveness of pharmacotherapeutic agents. The well-known saying of the English poet Alexander Pope that "Each person is different from another, and every day a person becomes different from yesterday" should become the "alpha and omega" in the observance of the principles of precision medicine.

A significant influence on the formation and progression of a tumor lesion is played by the functional microbiome, which has recently acquired the classified definition of a "wandering organ". It contains a significant number of additional markers and targets that can be aimed at improving technological innovations in oncological research of the patient's QoL roadmap [8]. Khondarar et al. [16] have developed the technology of low-invasive high-tech detection of cancer biomarkers. Identification of cancer biomarkers using microfluidic chipping, a phenomenon borrowed from the surrounding natural world, transforms fiction into reality.

Today, innovative technologies are becoming routine tools of evidence-based medicine, filling the space of intuitive medicine, which was mainly based on the principles of symptom complexes and integral diagnostic methods. The hand of the clock moving in the direction of the advantages of innovative technologies is only a manifestation of the work of a coordinated time mechanism, which is based on molecular-genetic omics technologies and is a precursor to the development and implementation of the paradigm of precision medicine, which can overcome numerous problems on the way to improving the patients' QoL [28—30].

Thanks to omics technologies, it is possible not only to characterize the structural and functional state of proteins, lipids, and their cooperative interaction but also to determine the immune repertoire in the tumor lesion creating prerequisites for the precision immunotherapy due to the activation of the patient's immune system aimed at destroying cancer cells. Until recently, the ratio of numerous cellular, chemokine-active, and other growth factors as the basis for dividing neoplasms into their "cold" and "hot" variants has not been taken into account. "Cold" tumors are characterized by low immunogenicity and respond weakly to immunotherapy, while "hot" tumors are more sensitive to inducers of antitumor defense. Therefore, immunotherapy holds more promise for certain groups of patients, and the proper evaluation of patients is required. This difference in response should be taken into account in treatment planning since this is a high-cost modality [31].

In the context of a personalized approach in the general strategy of treatment optimization, the issue of individualized nutrition of oncological patients becomes especially relevant, since age parameters and factors of endogenous and exogenous intoxication can significantly affect pharmacokinetic progress. The well-known saying of representatives of ancient medicine regarding food as a factor in therapy or poisoning acquires special importance for cancer patients. Today, there are quite a lot of recommendations for preventive nutrition, but there is a lack of specific dietary rations for patients with various nosologic forms of cancer, stages of cancer development, and especially in the conditions of chemotherapy. Ignoring the nutritional aspects causes additional turbulent processes in cancer patients, which provoke pronounced metabolic stress in the patient's body. The development and implementation of individual nutritional strategies can significantly in-

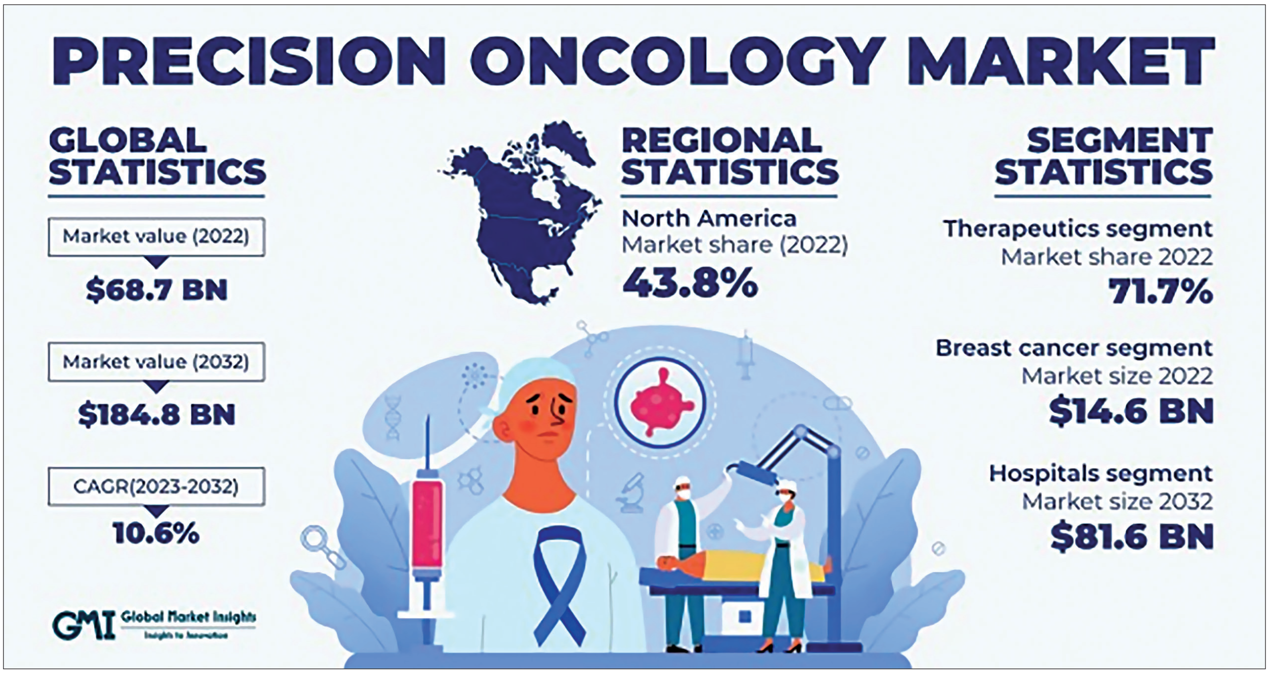

Fig. 2. The current state and growth forecasts of the precision medicine market in the next decade. *Note*: CAGR — Compound annual growth rate [42]

fluence the effectiveness of treatment and the QoL of patients [32—34].

However, the astronomical growth of knowledge about molecular genetic and general biological processes requires a deep analysis and synthesis of the obtained information and the development of an algorithm for their effective application. An optimal model of resource use, which is formed at the junction of systemic biology and the theory of complex systems, the features of which are difficult to explain from the viewpoint of individual components, is possible only under the conditions of the involvement of modern technologies of Artificial Intelligence (AI). AI will combine and harmonize the results of omics technologies: genomics, epigenomics, transcriptomics, interferomics, proteomics, metabolomics, and biomics and determine the hierarchy of the precision medicine algorithm at the current stage of development. It can be argued that if we imagine the pathways extending from the ancient medicine of Hippocrates, the philosophers Aristotle and R. Descartes, the inventor Robert Hooke, and the researcher Albert Kuhns to the author and founder of modern cybernetics and the science of management N. Wiener, these pathways are crossed at the stage of realizing a rational purposeful vision of the system for management of the functional state of a person [35—37].

The genesis of the symbiosis of medical-biological and cybernetic sciences aimed at processing information databases is simultaneously perceived thanks to simulation programs both as an object of research and as a subject of the process of learning the functioning of complex biological systems. Such opportunities allow for the processing of large volumes of data, avoiding the loss of information imperceptible to the human eye and generating significantly larger volumes of information necessary for finding an optimal solution. Combining the capabilities of AI tools with the quantitative and qualitative identification of molecular-genetic and structural-functional features of the cellular components can be a good example of optimizing the diagnosis of a malignant process and the effectiveness of choosing precision therapy. That is why improving the diagnosis of cancer, monitoring the course of the disease, and choosing the modern tools of therapy assisted by AI is becoming an extremely promising innovative technology in clinical practice. Today, the digital pathology tools are becoming a technological requirement in the development of personalized medicine, which is focused on extending life expectancy and improving the patient's QoL. In the structure of examination design and precision medicine strategy selection, the volume of research with the involvement of AI is growing rapidly. Thanks to the introduction of innovative technologies, the opportunities to-screen cancer occurrence at the stages of its preclinical manifestation, to create robotic remote monitoring technologies, to raise the level of therapy efficiency, and to expand the platform for the implementation of pilot projects to increase life expectancy and QoL are significantly increasing [38—40].

By 2030, precision medicine based on medical science will have covered large populations, which will make it possible, thanks to the design and analysis of the results of clinical genomics, to assess the patient's condition in a balanced way and calmly make effective decisions, so that the survival time and QoL could overcome the indicators of the present time bitter statistics [41].

The market of precision medicine in 2023 is to reach about 50% in North America, Europe, and the Asia-Pacific regions. In 2022, its volume accounted for over 70 billion dollars. According to the forecasts, it can reach over 180 billion dollars by 2032. The indicators of the market growth by 10.6% testify to the rapid dynamics of the implementation of the paradigm of precision medicine (Fig. 2) [42].

Today, for the sake of the dynamic development of the implementation of precision medicine based on innovative technologies, it is worth concentrating the efforts on the deep consolidation of transdisciplinary approaches that can form an algorithm of the new market of medical services for high QoL of cancer patients. This project should anticipate the development of the ways to achieve the goal involving a wide range of stakeholders, the implementation and use of modern tools, as well as providing the in-depth analysis and assessment of possible prospects and existing barriers for making balanced decisions.

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СУЧАСНИЙ ЛАНДШАФТ ІННОВАЦІЙНИХ ТЕХНОЛОГІЙ
В ОПТИМІЗАЦІЇ ЯКОСТІ ЖИТТЯ ОНКОХВОРИХ

В еру інтенсивного розвитку постгеномних технологій настав час для перегляду сучасної стратегії в подоланні проблем онкологічних хворих. В основу сучасного тренду нової парадигми закладено знання і можливості корекції молекулярно-генетичних процесів на засадах прецизійної медицини. Ключова роль у реалізації такого підходу належить сучасним інноваційним технологіям, серед яких особливе місце посідають омікс-технології. Зародження симбіозу медико-біологічних і кібернетичних технологій, спрямованого на обробку інформаційних баз даних, стає суб'єктом процесу пізнання функціонування складних біологічних систем. Сьогодні, задля динамічного розвитку впровадження прецизійної медицини на засадах інноваційних технологій, варто сконцентрувати зусилля на глибокій консолідації трансдисциплінарних підходів, здатних сформувати алгоритм нового ринку медичних послуг, спрямованих на підвищення якості життя.

Ключові слова: якість життя, прецизійна медицина, інноваційні технології, хворі на рак.