ejpmr, 2021,8(3), 105-106

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

THE ROLE AND PLACE OF CHEMOTHERAPY IN THE ERA OF TARGETED THERAPY AND IMMUNOTHERAPY

Alimkhodzhayeva L.T.*, Ziyavedenova S.S., Khodzhyaev A.V., Nigmanova N.A., Kasymov D.A., Makhmudova N.E., Zakirova L.T., Shamansurova N.S., Halimov Zh Zh. and Norbekova M.Kh.

Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology, MHRUz. Farobiy- 383.

***Corresponding Author: Dr. Alimkhodzhayeva L.T.**

Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology, MHRUz. Farobiy- 383.

Article Received on 05/01/2021 **Article Revised on 26/01/2021** **Article Accepted on 16/02/2021**

SUMMARY

This review analyzes the literature data on the role and place of chemotherapy in the era of the development of therapy and immunotherapy.

KEYWORDS: Immunotherapy, targeted therapy, chemotherapy, oncology.

Since the middle of the twentieth century, antitumor chemotherapy has strengthened its effective positions in everyday clinical practice, providing the possibility of curing some forms of leukemia, malignant lymphomas, germ cell and trophoblastic tumors, tumors of the Ewing sarcoma family, osteosarcomas, and childhood tumors. For some disseminated forms of solid tumors, it was possible to significantly increase the duration and quality of life. Despite the fact that the limit of the crude therapeutic potential of cytostatic agents has long been at its maximum, classical chemotherapy remains fairly well positioned in the world clinical guidelines as an adjuvant, neoadjuvant, curative and palliative option. Improving the methods of accompanying therapy has significantly improved the quality and effectiveness of cytostatic treatment, along with a decrease in its toxicity, including in elderly patients. Attempts to improve the effectiveness of targeted therapy of immune checkpoint inhibitors, the desire to maximize the benefits from the use of combinations of these drugs, as well as the creation of new agents aimed at complex modulation of immune responses, unfortunately, have not yet demonstrated bright and encouraging results. That is why the concept of apoptosis of tumor cells in previously studied chemotherapy regimens will for a long time be an active component of the treatment of cancer patients. Despite the abundance of studies devoted to the study of the effectiveness of targeted drugs and immunotherapy agents, until recently, work was actively carried out aimed at studying and improving adjuvant chemotherapy, in particular in patients with breast cancer. Studies of the efficacy of cytostatic agents in disseminated forms of tumors are still of great interest. Such reshaping of previously studied regimens resembles the story of continuous improvement of cytostatic therapy, which has significantly improved long-term treatment results. Alas, unresolved problems of dynamic heterogeneity of tumors and repopulation of tumor cells with genome instability and the ability to change under the pathogenic effect of the mutagenic action of cytostatics stand in the way of potential successes of chemotherapy. An attempt to move away from the generally accepted principles of classical chemotherapy, alternative methods of use towards cytostatics, allows us to instill some optimism regarding an increase in progression-free and disease-free survival, but not regarding the complete recovery of patients. Therefore, the concept of chronicity of the disease due to the sequential use of the studied options in the near future will prevail over the possibility of creating a universal drug that will instantly solve the problem of resistance. This is due not only to heterogeneity, but also to the lack of an integrated approach in the drug treatment of malignant diseases, which, ideally, should take into account the kinetics of tumor growth, microenvironment, homeostasis of the macroorganism, the dynamics of the genetic portrait of the tumor, epigenetic regulation, and other factors. That is why, throughout the history of the existence of anticancer drug therapy, we observe a stable principle of using combinations of registered drugs. The palette of successes and failures of this treatment concept is very diverse and is mostly represented by the addition of new agents to previously studied chemotherapy drugs.

Recently expressed interest has been aroused by the use of metronomic therapy, a strategy of chronic continuous administration of low doses of anticancer drugs with the aim of influencing not only tumor cells, but also the immunological microenvironment and angiogenesis. A feature of this method of treatment is its effectiveness regardless of the line of application. There is an assumption about the connection between various mechanisms of action of low doses of cytostatics with overcoming acquired resistance due to the effect on the

tumor microenvironment. In addition, the advantages of metronomic therapy are the absence of clinically significant toxicity and the possibility of using this method in elderly and somatically burdened patients. The renewed interest in metronomic therapy is also due to the possibility of its promising combination with IICP. Understanding the limits of the effectiveness of precision oncology and immunotherapy options opens up opportunities for further targeting patients for more effective use of chemotherapy. It is believed that chemotherapeutic agents promote the appearance of tumor antigens and initiate the attraction of cells of the immune system directly to the neoplasm. The concept of the ability of cytostatic therapy to alter the tumor microenvironment and increase the effectiveness of subsequent immunotherapy was demonstrated in the Voorwerk study, which included 67 patients with triple-negative metastatic breast cancer. Patients received nivolumab therapy either from the very beginning of treatment, or after induction of radiation or cytostatic therapy. Short-term use of cisplatin or doxorubicin has been found to significantly increase the likelihood of a response to immunotherapy. The administration of cytostatics was accompanied by reprogramming of the expression profile of genes involved in the regulation of the immune response.

With the currently available approaches in the arsenal of therapeutic and diagnostic options, disseminated cancer appears to be an incurable disease. Awareness of the listed problems of a clinical, scientific and pharmaco-economic nature in the field of oncology is the initial step in trying to solve these issues. An important role in increasing the chances of common and metastatic forms of malignant neoplasms for acquiring the status of chronic diseases with long survival is given to the consolidation of medical and scientific oncological communities, the development of clinical trials and the integration of their results into the practice of oncologists with active legislative and financial support from the state. Specifying the possibilities of solving these problems, we can single out the following set of aspects aimed at improving the results of treatment of disseminated forms of cancer:

1. Changing approaches to drug therapy in clinical practice (adaptive therapy, metronomic therapy and its combination with other agents, preventive combination therapy, intermittent therapy regimens, high-dose chemotherapy)
2. Initiation, active continuation and state support of research on the conversion of drugs into oncology, research on the integration of mathematical modeling to identify the optimal time and intensity of antitumor effects
3. Initiation, active continuation and government support of randomized phase III clinical trials aimed at exploring alternative approaches to treatment (adaptive therapy, metronomic therapy and its combinations with other agents, preventive combination therapy, intermittent therapy regimens, high-dose chemotherapy)
4. Active support and funding of laboratory research with their subsequent stepwise implementation in preclinical and clinical stages at the state level
5. Initiation, active continuation and state support of research aimed at studying immunology (manipulation of the microbiome, impact on the microenvironment, sensitization of tumors to IICP, new combinations for the induction and restoration of antitumor immune response, vaccine therapy)
6. Shifting the focus of scientific research goals towards biology of the tumor cell and its metabolism
7. Creation and maintenance of a global database of patients who showed exceptional response to treatment
8. National and international systems for data exchange and analysis of biosamples of patients
9. Improving systems for detecting molecular genetic disorders with an emphasis on circulating tumor DNA and its mutational status
10. Harmonization and reduction in cost of high-tech panels of wide profiling
11. Improving the legal and regulatory framework for the use of drugs outside the approved indications
12. Improving access to participation in precision therapy clinical trials.

REFERENCES

1. Jones P.A., Baylin S.B. The fundamental role of epigenetic events in cancer // Nat. Rev. Genet, 2002; 3: 415-428.
2. Zaletaev D.V., Strelnikov V.V., Nemtsova M.V., Babenko O.V., Kuznetsova E.B., Zemlyakova V.S. Methylation markers in the diagnosis of oncological diseases // Medical genetics, 2010; 9(1): 15-21.
3. Shkarpo (Rudenko) V.B., Tanas A.C., Kuznetsova E.B., Zaletaev D.V., Strelnikov V.B. Modern approaches to the screening of differential methylation of genomes of breast cancer cells // Medical genetics, 2009; 8(12): 41-45.
4. Baylin S.B., Esteller M., Rountree M.R. Aberrant pattern of DNA methylation, chromatin and gene expression in cancer // Hum. Mol. Genet, 2001; 10: 687-692-696.
5. Esteller M. Epigenetics in cancer // N. Engl. J. Med., 2008; 358: 1148-1159.
6. Chan A.O., Kim S.G., Bedeir A. et al. CpG island methylation in carcinoid and pancreatic endocrine tumors // Oncogene, 2003; 13: 924-934.
7. Jones P.A., Baylin S.B. The fundamental role of epigenetic events in cancer // Nat. Rev. Genet, 2002; 3: 415-428.
8. Fraga M.F., Esteller M. Hypermethylation of tumor-suppressing gene and diagnostics of oncological disease // Cancer, 2009; 45: 234-239.
9. McGregor G., Marley J. Methods of working with animal chromosomes. –M.: Mir., 1986; 268.