**Summary.** The work is dedicated to post-operative adjuvant therapy of melanoma. In 2012 in Kazakhstan, Kazakh Research Institute of Oncology and Eurasian Association of Oncologists (EAFO) initiated a multicenter controlled clinical research involving 186 patients for determining the comparative effectiveness of the use of alpha interferon and naderin and polychemotherapy – dacarbazine, cisplatin for skin melanoma of intermediate and high risk of progression.

**Keywords:** melanoma, alfa interferon, naderin.

**Relevance.** Skin melanoma is extremely malignant tumor and the most frequent cause of death among all skin diseases. The past 20 years were marked by a steady increase in incidence of skin melanoma among population in all regions of the world [1–4]. At the same time, according to national cancer register, in 2014 in Kazakhstan 2192 patients with skin melanoma were included into dispensary registry, and 316 new cases of this terrible disease were revealed. In spite of the fact that melanoma belongs to visually accessible localizations of a tumor, the specific weight of late stages (ІІІ–ІV) among patients with new cases remains quite high, fluctuating within 30–47% [1].

At early stages of development, it is difficult to distinguish melanoma from other pigmentary formations of skin; therefore, the accuracy of its diagnostics by doctors of general health network does not exceed 37–49%. The situation is aggravated with the fact that even among patients with "initial" forms of skin melanoma 45,6% of patients prior to treatment have clinically undefined intracutaneous, regional, remote metastases [1; 6–8]).

Standard method of treatment of this tumor is surgical. At timely identification on early, initial stages of melanoma development (stages I A and I B), surgical treatment is considered as an adequate method giving 80–90% of patients with 10-year mark with no symptoms of the disease [6-8]. At the same time, with the increase of tumor incidence at stages II and III the effectiveness of surgical method is sharply reduced and 50-80% of these patients die within the first two or three years from the moment of diagnosis [6].

Problems and failures of a surgical method are connected with development of local recurrence or regional and remote metastasis after operation [2-5]. The additional adjuvant therapies including radiation therapy, polychemotherapy, immunotherapy are used for the purpose of prevention of recurrence and metastasis.

The data obtained from randomized researches is quite contradicative and does not allow to completely evaluate the role and place of adjuvant immunotherapy p IF-a in prevention of recurrence and disease progression among patients with melanoma on stages II and III. All this has led to the fact that, despite some progress, preventive immunotherapy with alpha interferon is still not an officially approved type of adjuvant therapy of intermediate and high-risk skin melanoma in countries of Europe and CIS.

At the same time, high-dose mode of an immunotherapy with daily alpha interferon of 18 ml ME on m² (30-36 ml ME) within a year, used in the USA, was not widely used in Europe and the CIS countries due to toxicity and high cost of treatment. In addition, low-dose NFα modes used in Europe were not effective at high risk of disease progressing.

For determining uniform tactics, in 2012 the KazSRI of Oncology initiated a multicenter controlled clinical trial to evaluate the efficiency of adjuvant immunotherapy with alpha interferon and naderin with participation of EAFO expert group.

**The research protocol was discussed and approved on:**

1. EAFO-international conference – Adjuvant therapy of skin melanoma. Moscow, Russia, June 2011.
3. Meeting of the working group of employees of chemotherapy, oncological urology and bone and soft tissue tumors departments of Kazakh Research Institute of Oncology and Radiology in Almaty, Kazakhstan, January 2012.

**Expert group of the research.**

2. S. Agarwala (USA) – Director of Immunology Program at the Oncological Center of St. Looney. The head of the E 1697 research of melanoma committee in Eastern Cooperated Oncology Group (ECOG).
3. Demidov LV (Russia) – Head of the Biotherapy Department of Scientific Research Institute of clinical oncology RONC of N.N

4. Somasundranap S. (India) – EAFO Director (Association of Oncologists of Europe and Asia)

**Goal of the research.** Improvement of results of surgical treatment of skin melanoma.

**Research objectives**

1. To evaluate the efficiency of immunotherapy with alpha interferon in combination with naderin for skin melanoma of intermediate and high risk in adjuvant mode compared with polychemotherapy.

2. To assess the dynamics of cellular immunity indicators and tumor marker levels of S-100 in treatment of skin melanoma of high and intermediate risk of progression.

3. To declare the most effective scheme of adjuvant treatment based on results taking into account the major prognostic factors.

**Materials and methods of the research.** The material for the research is data on 186 oncological patients with skin melanoma treated in KazSRI of oncology and radiology within the multicenter randomized research EAFO from 2012 to 2016. After surgical treatment, all patients had histologic examination of a tumor with definition of invasion degree of skin layers, existence of lymphoid infiltration and existence of ulceration. Then the patients were brought through randomization (“blind” division into two groups), where the main group was included into high-dose immunotherapy by alpha interferon 2B (“Intron-A”) in combination with naderin, and the control group patients after operation received chemotherapy according to the scheme: dacarbazine 1400 mg, Cisplatinum 50 mg; median (duration) of disease-free period has made 11,7±3,1 months.

Analysis of the results showed that skin melanoma among patients who have received preventive courses of chemotherapy after surgical treatment according to the scheme – Dacarbazine 1400 mg, Cisplatinum 50 mg; median (duration) of disease-free period has made 11,7±3,1 months. During immunotherapy with alpha interferon 2B (Intron-A) of 18 million units in combination with naderin, disease-free period has made 26,08 months.

Thus, the comparative analysis of adjuvant chemotherapy and immunotherapy has shown advantage of an immunotherapy for 4 months in comparison with chemotherapy. High doses of interferon in combination with naderin keep anti-proliferative property – but due to naderin, they are better tolerated; considerable decrease was noted in toxicity, leukopenia and immunodeficiency in comparison with polychemotherapy.

**Conclusions**

1. Adjuvant therapy of melanoma according to literature remains an unsolved problem of clinical oncology.

2. Data of foreign randomized researches of the USA and Europe are contradictory; therefore, there is no uniform standard of adjuvant therapy for melanoma of intermediate and high-risk.

3. The most promising line of adjuvant treatment of melanoma of skin melanoma according to EAFO is the combination of alpha interferon with naderin allowing to reduce toxicity, to increase efficiency and tolerance of high doses of alpha interferon and to raise the disease-free period in comparison with chemotherapy from 11,7±3,1 months to 26,08±3,1 months (р<0,05).

4. Skin melanoma is a heterogeneous tumor and it requires further search of predictive factors – biological features of both the tumor, and patient’s body functions

5. Definition of the optimum schemes of treatment and development of a uniform standard requires performing of multicenter controlled clinical researches, including Kazakh Scientific Research Institute of Oncology and Radiology and all regional oncological clinics of Kazakhstan.
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