

STATEMENT

FROM PROF. KRASIMIR IVANOV, MD, PHD, DSC.

Chairman of the Scientific Jury

appointed with Ordinance № P-109-263/ 21.07.2020 г.

from the Rector of Medical University "Prof. Paraskev Stoyanov" - Varna

Concerning: Dissertation thesis from Dr. Jeliazgo Iliiev Arabadjiev for acquisition of the educational and scientific degree "Doctor" in Medical University "Prof. Paraskev Stoyanov" - Varna, Department of Oncology entitled "PREDICTIVE AND PROGNOSTIC VALUE OF TUMOR-INFILTRATING LYMPHOCYTES IN WOMEN WITH BREAST CANCER" with scientific supervisor Assoc. Prof. Eleonora Dimitrova-Gospodinova, MD, Ph.D.

The topic of the dissertation is contemporary and dissertable, considering the problem of the most common malignancy in women, namely breast cancer (BC) and the ability to assess the prognosis and response to treatment based on tumor-filtering lymphocytes (TILs).

The dissertation consists of 118 pages and is illustrated with 31 figures and 21 tables in 9 chapters: literature review, research methodology, research results, discussion, conclusions, contributions, applications, publications on the topic and literature used. The bibliography includes 246 titles, of which 1 in Bulgarian and 245 in English.

The review of the literature review occupies 54 pages. The dissertation has examined in detail the epidemiology, etiology / genetics, diagnosis, classification and treatment of breast cancer. Particular attention was paid to the main aspects of the immunological response against tumor cells, the results of clinical studies in which the prognostic and predictive role of tumor-filtering lymphocytes (TILs) were evaluated. The methodology for assessing the degree of stromal lymphocytic infiltration is also well described. All this shows that the author has studied the literary sources well enough and is acquainted with the available publications on the subject.

The author sets a clearly stated goal, namely: to study the degree of TILs in patients with breast cancer in order to establish their prognostic and predictive value and the possibility of specific application in practice. To achieve the set goal, 6 tasks were performed, using the following methods: diagnostics, pathoanatomical methods and methods of statistical analysis.

Dr. Jeliazgo Arabadjiev examined retrospectively the documentation of 118 patients who went through the medical oncology department of Acibadem CityClinic Tokuda Hospital EAD and after a thorough examination of the anamnesis for final study were selected 58 women included in the analysis. The study was conducted for the period from January 2019. until January 2020. All patients were histologically verified with stage I-VI breast cancer and received surgical, systemic, or radiation therapy between 1997 and 2020.

The problem of prognostic and predictive value of the degree of tumor-infiltrating lymphocytes in breast cancer has been examined in detail and the dissertation has indicated in which stages of the disease, in which histological and immunohistochemical (ICH) subtypes, in which types of treatment this indicator can be a reliable marker. Correlations between the degree of tumor lymphocyte infiltration and the overall survival (OS) and the time of survival

without an event, depending on the development of the disease, age, the location of the primary tumor, the performed adjuvant radiotherapy were studied.

The conclusions are 9 and represent a strictly differentiated synthesis of the overall development and meet the goals and objectives.

As contributions to the dissertation, grouped into two categories, I can admit:

I. Contributions of original value

1. For the first time in Bulgaria a study of the dependence of OS and the degree of TILs in BC is conducted.
2. From the conducted correlation analyzes for the first time in Bulgaria data for connection between degree of TILs and OS depending on ICH status are reported, as the prognostic value of TILs in HR + / HER2-negative patients with BC is statistically confirmed.
3. For the first time in Bulgaria, statistically significant results of an analysis are reported, which confirms the predictive value of TILs compared to the treatment performed with the sequential application of CT and ET or CT and ET as a stand-alone treatment for BC.
4. For the first time there is a tendency for correlation between the degree of TILs and performed ALL and their impact on OS in patients with BC.

II. Contributions of scientific and practical nature

1. Determination of the degree of stromal tumor lymphocyte infiltration in primary tumor material or from hematoxylin-eosin-stained metastasis may be the subject of further studies to confirm a potential correlation for response to drug and radiation antitumor treatment in BC as predictive biomarker.
2. Creating a prerequisite for developing a recommendation for escalation or de-escalation of chemotherapy or adjuvant radiotherapy in breast cancer based on the degree of tumor infiltrating lymphocytes.

Author's abstract consists of 44 pages and contains the main chapters as in the dissertation thesis.

The dissertation has published 6 scientific articles on the topic of the dissertation, being the sole author in 5 of them and the first author in 1 of them. A presentation on the topic of a scientific forum on oncology in the country was given.

The dissertation of Dr. Jeliazgo Arabadjiev on "Predictive and prognostic value of tumor-filtering lymphocytes in women with breast cancer" is a fully completed, well and properly structured dissertation that meets the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria, the regulations for its application and the regulations of the Medical University - Varna.

Due to the above, I fully believe my positive assessment of the dissertation I propose to the highly respected Scientific Jury to award Dr. Jeliazgo Iliiev Arabadjiev an educational and scientific degree "DOCTOR".

**Prof. Krasimir Ivanov, MD, DSc.
Chairman of the Scientific Jury**

