



STATEMENT

By Prof. Dr. Yana Dimitrova Bocheva, PhD

Head of the Department of Clinical Laboratory

MU "Prof. Dr. Paraskev Stoyanov", Varna

Member of the Scientific Jury, appointed by order No. R- P-819/03.04.2023 of the Rector of the Medical University -Plovdiv

Subject: PhD thesis of Dr. Snezhana Stoyanova Stoencheva, doctoral student of independent training in the "Clinical Laboratory" doctoral program, conducted in the Department "Clinical Laboratory", Faculty of Pharmacy in Medical University of Plovdiv for the acquisition of an educational and scientific degree "PhD" in the field of higher education 7. Health care and sports, professional direction 7.1. Medicine and Doctoral Program "Clinical Laboratory", with scientific supervisors assoc. prof. Tanya Deneva, MD, PhD and prof. Janet Grudeva-Popova, MD, PhD.

On the basis of Order No. R-819/03.04.2023 of the Rector of the Medical University of Plovdiv and the decision of the Scientific Jury, confirmed by the above-mentioned order, I have been assigned to prepare an opinion for a dissertation work on the topic "Clinical-laboratory evaluation of coagulation and fibrinolysis in patients with malignant diseases" by Dr. Snezhana Stoyanova Stoencheva.

The statement is prepared in accordance with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria. The presented documents are in accordance with Art. 70 (1) of I. Section. Acquisition of educational and scientific degree "DOCTOR" in MU-Plovdiv; Regulations of MU-Plovdiv dated 28.01.2021. The doctoral student has attached 3 full-text publications and 7 participations in national and international forums with published summaries on the topic of the dissertation work. All stages of the procedure have been observed, there is no change to the original topic and supervisor.

Brief biographical details of the applicant

Dr. Stoencheva graduated from Plovdiv Language High School, English profile in 1999. She graduated from Medical University - Plovdiv in 2006. with a master's degree in medicine. She acquired a specialty in clinical laboratory in 2013. Dr. Stoencheva began her professional development as a physician in MDL "Astralab" OOD - Gorna Oryahovitsa in 2007. Since 2012 she is a resident in the Central Clinical Laboratory of UMBAL "St. Georgi" EAD, Plovdiv, and since 2015- an assistant at the Department of Clinical Laboratory at the Medical University - Plovdiv, Faculty of Pharmacy.

Since June 2021, she is a doctoral student of independent training in the "Clinical Laboratory" doctoral program at the same department. Her teaching responsibilities are : guidance of practical exercises in clinical laboratory for students of the specialty "Medicine", III year - in Bulgarian and English, optional courses for students of the specialty "Nursing", I year and practical exercises in clinical chemistry for students from the specialty "Pharmacy", III year. The doctoral student declared participation in 4 intra-university scientific projects, authorship in 10 articles and one teaching aid and 13 citations. Fluent in English. She is a member of the Bulgarian Medical Union and the Bulgarian Clinical Laboratory Society.

Relevance of the topic

The topic of the presented dissertation work has been selected carefully according to the personal clinical interests of the PhD student and the accumulated expertise and direction of the scientific supervisors.

Modern diagnostic medical specialties, to whose rapid development we include the clinical laboratory, have directed their efforts, in addition to the validation and routinization of new laboratory, genetic and molecular markers, and in search of new projections of known parameters.

Epidemiological data determine the social significance of oncological diseases, and resources from all clinical and diagnostic specialties are directed to their prevention, diagnosis, and therapy. Thrombosis is a well-known and common complication in patients with malignancies and contributes significantly to morbidity and mortality in these patients. The relationship between malignant diseases and thrombosis has been a problem of scientific research since the 19th century, and now it is indisputable that tumor pathology is associated with a 4-fold higher risk of thrombosis, and systemic chemotherapy increases this risk up to 7-fold.

In our country, there are still no systematic studies that focus on the clinical-laboratory evaluation of deviations in the hemostasis system in oncological diseases. A logical result of this information vacuum in our country at the present time is the scarce data and scientific publications, which arouses the research interest of the dissertation student and scientific supervisors.

In this context, I consider the conceptual project of this PhD thesis presented to me for evaluation to be current in conception, prospective in terms of publication results, and at the same time classical in methodological implementation.

Characteristics, volume, structure, and content of the dissertation

The dissertation is set out on 129 pages, including: Introduction - 2 pages, Literature review - 25 pages, Aim and tasks - 1 page, Materials, and methods - 14 pages, Results - 58 pages, Discussion - 7 pages., Conclusions - 1 page, Contributions - 1 page, Publications - 2 pages, Bibliography - 18 pages. The presentation consists of 24 tables and 71 figures. The bibliography contains 252 sources, of which 3 are in Cyrillic. The latter includes contemporary sources, 47% of which are from the last 10 years.

The structure of the dissertation corresponds to the modern concepts of the structure of the dissertation without bias towards theorizing or methodological excesses with an emphasis on the results and with a brief interpretation. A clear style is demonstrated, with an excellent usage of highly specialized terminology.

The literature review is logical and well structured, consistently defining the clinical problem of thrombosis and its epidemiological characteristics and passing through its specific manifestations/Pulmonary embolism/ and commenting on possible therapeutic solutions/anticoagulant therapy/ as an additional treatment to systemic chemotherapy. The text includes physiological and propaedeutic data on the mechanisms of hemostasis, angiogenesis, carcinogenesis, and fibrinolysis, and focuses on the relevant parameters to assessing the close relationship between coagulation and tumor progression.

The aim is clearly formulated and is a logical consequence of the summary of the literature review, it corresponds to the title and is specified by the text of the tasks of the dissertation work.

The dissertation is designed with the formulation of five tasks, with the first task being entirely practical, the second, third and fifth tasks having an analytical nature, and the fourth, determining the diagnostic reliability of the studied indicators, can be characterized as basically laboratory.

Material and methods

The design of Dr. Stoencheva's study is single-center, prospective, controlled, and longitudinal. It includes 185 persons between the ages of 18-70 of Bulgarian nationality: 120 patients from the medical oncology clinic and radiotherapy clinic at UMBAL "St. Georgi" - Plovdiv, divided into 3 patient groups: mammary gland carcinoma (n=38), lung carcinoma (n=42) and non-Hodgkin's lymphoma (NHL) (n=40) and a control group of 65 clinically healthy volunteers (30 women and 35 men).

The study was approved by the Committee on Scientific Ethics at the Medical University of Plovdiv with decision No. R-1722/12.03.2018. The clinical and laboratory tests were carried out in the Clinical Laboratory of the UMBAL "St. George", the city of Plovdiv. The laboratory methods used are standardized, automatic hemocoagulation methods (chronometric, immunoturbidimetric, chromogenic), ELISA methods, hematological and clinical-chemical analyses, which are described precisely and in detail.

Results

In a total of 58 pages, Dr. Stoencheva describes in detail and sequentially the implementation of each of the tasks, leading to the fulfillment of the formulated aim of her scientific work. 24 tables and 71 figures have been compiled, accompanied by an understandable text, and the applied statistical methods of analysis have been correctly selected and correctly interpreted. For each of the clinical groups, demographic data, results of the selected clinical and laboratory indicators for coagulation and fibrinolysis are listed. A comparative analysis of the results compared to healthy controls was performed, their dynamics and changes during the treatment were evaluated per visit. This is followed by an analysis of the correlation between hemostasis indicators in patients and controls and an assessment of their diagnostic reliability.

In the "**Discussion**" section of the dissertation, Dr. Snezhana Stoencheva makes an objective analysis of her results, comparing them with those of other scientific groups, observing the order of the presented results, the logic of her presentation and keeping the guiding line of the set aim and tasks. It is in this chapter of the dissertation work that the good level of preparation of the dissertation student is evident. She demonstrates knowledge of the Bulgarian and international resources on the problem under consideration, as well as the ethical and critical attitude towards her own results.

I fully agree with the defined 7 **conclusions** that reflect the results obtained. They are formulated clearly and specifically. They have the support and evidential material in the "Results" chapter of the dissertation work.

The dissertation ends with the definition of 5 **contributions**, of which three are original and one is confirmatory. Contribution 5 I consider poorly expressed and stylistically inappropriate.

Publications and announcements on the subject

A list of 3 full-text publications in international journals and 7 participations in scientific forums are presented - 5 international conferences, 1 national conference, 1 regional university forum. Dr. Stoencheva is the first author on all full-text publications. The scientific activity of the dissertation student is in accordance with the Law on the Development of the Academic Staff of the Republic of Bulgaria and the regulations for its application at MU-Plovdiv.

The **abstract** (50 pages) has been developed and structured according to the requirements, and its content fully corresponds to the dissertation work.

Conclusion

The PhD thesis of Dr. Snezhana Stoyanova Stoencheva is essentially a scientific research with a practical orientation. The topic is current, interesting, and challenging. The applied methods are adequate to achieve the set aim and tasks, the results are significant, and the conclusions are logical and correctly drawn. Contributions are original and practical. Dr. Stoencheva invested a lot of work, patience and persistence in the development of this research.

The dissertation on the topic "Clinical-laboratory assessment of coagulation and fibrinolysis in patients with malignant diseases" authored by Dr. Snezhana Stoyanova Stoencheva, covers the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its implementation and the relevant regulations of the Medical University of Plovdiv. The presented materials and dissertation results fully correspond to the specific requirements adopted in connection with the Regulations of the Medical university of Plovdiv for the application of the Law on the Development of the Academic Staff in the Republic of Bulgaria.

Based on the presentation, I give a positive assessment of her dissertation work and recommend to the honorable jury to award Dr. Snezhana Stoyanova Stoencheva the educational and scientific degree "DOCTOR" in the doctoral program in Clinical Laboratory.

05.05.2023

Varna

Prof. Dr. Yana Dimitrova Bocheva, MD, PhD

Заличено на основание
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