# OPINION

## By Assoc. Prof. Dr. Svitlana Yurievna Bachurska, MD

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Regarding: Dissertation for the procedure for acquiring of the educational and scientific degree "doctor" in the field of higher education 7. "Healthcare and Sports", Professional field 7.1. "Medicine", Scientific specialty "Internal Diseases".

**By Dr. Tanya Lyubomirova Zlatanova,** PhD student of self-training at the Clinic of Medical Oncology at Acibadem City Clinic UMHAT "Tokuda" Sofia (Order for enrollment 15-05-139/30.09.2022).

**Title: "Markers for Systemic Inflammation and Efficacy of Immunotherapy in Patients with Metastatic Non-Small Cell Lung Cancer".**

**Scientific supervisor - Assoc. Prof. Dr. Zhelyazko Arabadzhiev, MD.**

## General Presentation of the Procedure and the PhD Candidate

The presented set of materials on electronic media complies with the Regulations for the conditions and procedures for acquiring scientific degrees and holding academic positions at Acibadem City Clinic UMHAT "Tokuda" Sofia. Attached are the dissertation, the abstract, and a total of 4 publications related to the dissertation.

## Relevance of the Topic

The topic is contemporary and extremely relevant, addressing a problem of significant scientific and practical importance, namely the validation of easily calculable prognostic indices and scores that can easily identify patients at high risk of thrombosis and death. A clear and specific goal is defined – "to investigate the prognostic potential of the Systemic Immune-Inflammation Index (SII), Khorana score (KS), modified Khorana score (mKS), and the Inflammatory Index in advanced NSCLC (ALI) regarding therapeutic response and survival during first-line immunotherapy or chemoimmunotherapy in patients with metastatic non-small cell lung cancer".

## Understanding of the Problem

The literature review presents in a synthesized form the demographic distribution of lung cancer on a global and national scale, the main aspects of the etiology and pathogenesis of lung carcinoma, its histological and molecular-genetic specifics, and staging. Prognostic and predictive factors in lung cancer are described in detail. The PhD candidate emphasizes inflammatory markers as a negative prognostic factor and their inclusion in prognostic indices

and scores. Current therapeutic strategies for lung cancer are thoroughly presented. The literature review concludes with a brief analysis of the reasons for the increased risk of thrombosis and the role of systemic inflammation in carcinogenesis and maintaining an active tumor process.

**Research Methodology**

The methods used are chosen in accordance with the set goals and tasks. The methodology of the conducted research is thoroughly described and systematically illustrated. The described methods and their application suggest the achievement of adequate results.

**Characteristics and Evaluation of the Dissertation and Contributions**

The dissertation is written on 132 pages, starting with a brief introduction on 1 page. The literature review is written on 42 pages with sufficient depth and comprehensiveness, structured into nine sections and ending with a brief analysis directing towards defining the goal of the dissertation. The goal of the dissertation is clearly and precisely formulated, corresponding to the topic of the dissertation. To achieve the goal, six tasks have been set, marking the main stages of the study. The number of patients studied (188) is sufficient to achieve adequate results. Clinical, diagnostic, therapeutic, and statistical methods were used for the study. The methodological part is demonstrated on 10 pages, described in sufficient detail, showing good knowledge and professional mastery of the methods used.

**Results of the Study**

The results of the conducted studies correspond to the set tasks. They are written on 43 pages. The results of task 1 illustrate the clinical and laboratory characteristics of patients with metastatic NSCLC treated with first-line immunotherapy or combined chemoimmunotherapy. The results of tasks 2 and 3 illustrate the correlation and prognostic potential of SII, KS, mKS, ALI in the two groups studied before the start of treatment regarding tumor response, progression-free survival, and overall survival. The results of task 4 define the role of Khorana score, modified Khorana score, and SII score as prognostic markers for the occurrence of thrombosis. The results of task 5 provide information on the frequency and type of immune-mediated toxicities. The results of task 6 illustrate the relationship between systemic inflammation markers (KS, mKS, SII, and ALI) and early death. Chapter 3 contains 39 figures and 60 tables that give a clear and concise nature to the dissertation. The obtained results are discussed and analyzed in Chapter 4, written on 13 pages, presenting a critical review of the obtained results and a comparison with the data described in the literature on the studied issues. The dissertation concludes with the formulation of conclusions and recommendations regarding the set tasks.

The dissertation contains 198 literature sources, most of which are recent, published in the last few years in referenced and cited editions.

**Evaluation of the Publications and Personal Contribution of the PhD Candidate**

A total of 4 scientific publications related to the dissertation, published in the Bulgarian periodical press, are presented. The PhD candidate is the first author in 2 of them.

**Critical Remarks**

Most of the conclusions and recommendations represent indisputable contributions of the dissertation both theoretically and scientifically-practically and deserve to be presented in a separate chapter "Contributions".

**Abstract**

The abstract is of sufficient volume, well-structured, and illustrated with tables and figures, in accordance with the main requirements for content and layout. Its content fully and accurately reflects the main results of the dissertation.

**Conclusion**

Based on the above, I believe that the dissertation of Dr. Tanya Lyubomirova Zlatanova represents a fully completed scientific product with scientifically applicable and, above all, clinically significant contributions. The dissertation fully complies with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria for the acquisition of the educational and scientific degree "doctor".

Therefore, I give my **positive** assessment of the overall work of the PhD candidate and propose to the honorable scientific jury **to award the educational and scientific degree "doctor" to Dr. Tanya Lyubomirova Zlatanova in the doctorate program "Internal Diseases".**

16.08.2024 г.

Sofia

Assigned by:/.........................

/Assoc. Prof. Dr. Svitlana Bachurska, MD/