

TO
THE CHAIRPERSON OF THE SCIENTIFIC JURY,
APPOINTED BY ORDER № 15-05-92/11.07.2024
OF THE EXECUTIVE DIRECTOR AND THE PROCURATOR
OF "ACIBADEM CITY CLINIC UMHAT TOKUDA" EAD,
AND BASED ON THE DECISION OF THE SCIENTIFIC COUNCIL/
PROTOCOL №53/26.06.2024/

OPINION

By Assoc. Prof. Lachezar Boyanov Lozanov, PhD,
Head of the Department of Internal Medicine (Endocrinology and Nephrology),
"Acibadem City Clinic Tokuda University Hospital" EAD

Regarding the dissertation on the topic: **"MARKERS FOR SYSTEMIC INFLAMMATION AND EFFICACY OF IMMUNOTHERAPY IN PATIENTS WITH METASTATIC NON-SMALL CELL CANCER",**

submitted for the acquisition of the educational and scientific degree "PhD" in the field of Higher Education 7. Healthcare and Sports, professional field 7.1. Medicine, PhD program "Internal Medicine,"

by **Dr. TANYA LYUBOMIROVA ZLATANOVA**, a PhD candidate of independent preparation at the Department of Medical Oncology, "Acibadem City Clinic Tokuda University Hospital" EAD,

Scientific supervisor: Assoc. Prof. Jeliazko Iliev Arabadjiev, PhD.

Dear Members of the Academic Committee,

Dr. Tanya Zlatanova's dissertation, concerning the effectiveness of immunotherapy in patients with lung cancer, is dedicated to the modern treatment of one of the socially significant problems in clinical oncology, which leads to severely impaired quality of life and increased mortality in such patients. The efficacy of contemporary therapies, such as immunotherapy, is

a crucial prerequisite for successful treatment. In addition to early diagnosis, it is essential to search for specific biomarkers that allow for patient stratification. This would enable an individualized approach to treatment, monitoring the patient's response, and determining the prognosis of the disease with greater accuracy. The prognostic potential of the Systemic Inflammation Index (SII), Korana score, and the Inflammatory Index in advanced NSCLC (ALI), as examined in this dissertation, in terms of survival and therapeutic response, is of great importance. This is also the main goal of Dr. Tanya Zlatanova, which she has successfully realized through the tasks she has set out. The role of these indicators in the prognosis and treatment response is proven. The author's results also demonstrate the relationship between the studied markers of systemic inflammation, mortality, and the frequency of immune-mediated toxicity during treatment.

The dissertation comprises a sufficient volume of 132 standard pages, adhering to the fundamental sections typically required for a dissertation, and is well-illustrated with 39 figures and 60 tables. It cites 198 references, 1 from Bulgarian authors and 197 from international authors, and is correctly formulated and structured.

The objective is clearly and precisely formulated. A large cohort of patients—188 in total has been studied. The six objectives set out have been successfully achieved, and the analysis of the obtained results has allowed for the fulfillment of the stated goal.

Ten conclusions and nine contributions have been drawn, of which five are original with significant scientific potential, and four have practical-scientific value. For the first time globally, the role of the modified Korana score (mKS) and the Systemic Inflammation Index (SII) as factors for early mortality (within six months of starting monotherapy or combination chemo-immunotherapy) in patients with metastatic NSCLC has been investigated. For the first time in Bulgaria, the role of systemic inflammation markers SII, KS, mKS, and ALI as prognostic factors for progression-free survival (PFS), overall survival (OS), and tumor response in patients with metastatic NSCLC who received first-line monotherapy or combination chemo-immunotherapy has been examined. Furthermore, for the first time in Bulgaria, the role of SII, KS, mKS, and ALI concerning the risk of thrombosis development has been studied. A study with prospective monitoring of patients with metastatic NSCLC, examining albumin and D-dimer levels in blood before systemic therapy initiation to assess cancer cachexia and thrombosis risk, has also been conducted for the first time in Bulgaria. Additionally, the frequency and types of immune-mediated toxicities during first-line

monotherapy or combination chemo-immunotherapy in patients with NSCLC have been investigated and described for the first time in the country.

The abstract adheres to academic standards and corresponds to the content of the dissertation. The doctoral candidate has systematically contributed to four original publications on the subject, has presented at both national and international scientific conferences, and has met all necessary requirements.

CONCLUSION:

The submitted documents and dissertation **“MARKERS FOR SYSTEMIC INFLAMMATION AND EFFICACY OF IMMUNOTHERAPY IN PATIENTS WITH METASTATIC NON-SMALL CELL CANCER ”** meet all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for the Implementation of the LDASRB, and the specific requirements adopted in connection with the Regulations of “Acibadem City Clinic Tokuda University Hospital” EAD. No plagiarism has been detected.

Dr. Tanya Zlatanova's dissertation is current and well-structured. The design of the individual studies and the overall framework of the research align with the objectives and tasks. The materials and methods are well-chosen and meticulously executed. The conclusions are well-grounded and stem from the obtained results.

In light of the above, I confidently give a positive assessment of the dissertation and recommend to the esteemed Academic Committee that the educational and scientific degree "PhD" in the field of Higher Education 7. Healthcare and Sports, professional field 7.1. Medicine, PhD program "Internal Medicine" be awarded to Dr. Tanya Lyubomirova Zlatanova, for which I vote in favor.

Sofia, 03.09.2024

Prepared by:



Assoc. Prof. Lachezar B. Lozanov, PhD
Head of the Department of Internal Medicine