

STATEMENT

From Associate Professor Zhelyazko Iliev Arabadzhiev, MD, PhD
Head of Department of Medical Oncology, Adibadem City Clinic UMHAT Tokuda EAD,
Sofia

According to Order № P-109-121 / 16.02.2023 of the Rector of the Medical University – Varna and Protocol № 81 / 06.02.2023, I have been selected to prepare an opinion on the dissertation of Dr. Teodorika Vitalinova Panayotova

Regarding the dissertation thesis entitled:

"Impact of distance and travel time to cancer center on lung carcinoma treatment outcomes "

for awarding educational and scientific degree "Doctor" in the field of higher education: 7. Health and sports, professional field 7.1 Medicine and specialty "Oncology", code 03.01.46.

Author: Dr. Teodorika Vitalinova Panayotova

Scientific supervisor: Assoc. Prof. Nikolay Vladimirov Conev, MD, PhD

1. Significance of the problem and formulation of the aim and objectives:

Lung cancer is the second most common malignant neoplasm after breast cancer in women. As for the male sex, lung carcinoma occupies a leading position in terms of frequency of occurrence. Despite modern strategies to combat the disease, lung cancer continues to be the leading cause of cancer-associated deaths in both sexes. The economic level of development of a country has no impact on male mortality, but there is a higher mortality rate for women in highly industrialized countries than those in developing ones. All these data justify the conclusion that lung carcinoma is a disease of a socially significant nature and as such should be a priority for healthcare professionals. Prolonging patient survival, increasing therapy effectiveness, improving quality of life and diagnostic and treatment approach are subject to spending significant resources of financial, intellectual and technological nature.

The therapeutic approach of cancer patients rests on evidence-based medicine rather than empirical experience of the individual physician. The main focus is the so-called multidisciplinary approach, determining the participation of a large number of qualified specialists (surgeons, oncologists, pathologists, radiotherapists, etc.) in the diagnosis, treatment and even for palliative purposes in lung cancer. Centralization, as a phenomenon of global and impactful nature, has a direct influence on the health system. Location of most university multiprofile hospitals with a large range of medical activities offered in larger

settlements poses a relatively rarely discussed problem for patient transport to treatment facility and how distance affects therapy outcomes and even life expectancy.

For these reasons, the dissertation of Dr. Teodorika Panayotova focuses on a topical problem for modern medicine and has applications from both a theoretical and practical point of view.

The purpose of the dissertation is clearly formulated, and the objectives are inherently logical steps, the content and consistency of which fully serve the specified aims.

2. Dissertation structure:

The dissertation has a classical structure. It is presented by 118 pages, of which: Introduction - 2 pages, Literature Review - 58 pages, Aim and objectives - 1 page, Hypotheses - 2 pages, Materials and methods - 1 page, Results - 9 pages, Discussion - 10 pages, Summary - 3 page, Conclusions - 1 page, Contributions - 1 page, Publications and participations in scientific forums related to the dissertation - 3 pages. The dissertation is illustrated with 6 tables and 15 figures. The bibliography includes 259 titles, of which 1 in Cyrillic and 258 in Latin.

The structure of the dissertation has the appropriate logical background and consistency, is well balanced and meets the requirements of the Law on the Development of Scientific Staff in the Republic of Bulgaria.

3. Literary awareness of the dissertation:

The literature review is written expertly and thoroughly. It is based on a large volume of studied literature, which allows consideration of epidemiology, risk factors, etiology, genetic predisposition, diagnosis and treatment in depth. A major place is devoted to the role of the multidisciplinary team in diagnosis and treatment, as well as the influence of time and distance as factors of prognostic and predictive value. Scientific publications on the topic have been carefully selected and analyzed in detail. They are approached with the necessary criticality. The main problems and unresolved issues in this direction are outlined.

The impressive amount of information used by the dissertant, the correct use of scientific terminology, as well as the full and correct citation of authors of scientific publications in the field is impressive. It is necessary to focus on the precise orientation and pragmatized comprehensiveness of the literary review, which defines Dr. Panayotova as a complete researcher with a multifaceted view of the consideration of a specific problem. The bibliography includes 259 literary sources. The relevance of the literature used is very impressive, with most of the cited sources being from the last 10 years.

The aim of the dissertation is a logical continuation of the literature review, namely: *"To investigate the impact of distance and travel time to cancer center on lung carcinoma treatment outcomes."*

There are nine main objectives set, which are clearly formulated and consistent with the aim. This reflects the excellent theoretical background and in-depth understanding of the problem by the doctoral student.

4. Methodological level and research design:

After the clearly defined aims and objectives, the author puts forward the hypothesis on which the scientific work rests. For precise selection of the respective patient population studied, strictly defined inclusion and exclusion criteria are set. The dissertation is based on a retrospective single-center analysis of 9240 patients with histologically verified lung cancer. The survey covers the period 2005 to 2020. The methods applied for statistical analysis of the results obtained are described in depth and subdivided into two categories for the sake of clarity.

5. Consistency between aim, results and conclusions

Between the set aim, the results obtained, the discussion and the conclusions drawn, there is a logical unity. The results are presented in detail and illustrated with the corresponding graphs, figures and tables. The discussion reflects the dissertant's critical opinion towards the scientific work and is an in-depth analysis of both the advantages and disadvantages of the conducted research. Creative hypotheses are presented that raise additional questions and direct the eyes to new horizons for conquering. After the analytical discussion, the conclusions follow, which are clearly formulated and supporting the author's hypothesis.

6. Analysis of conclusions and contributions:

Based on the results obtained, the author synthesized 7 specific conclusions, which are clearly formulated and have a meaningful relationship with the set aim and the developed objectives. The conclusions of the study on travel burden impact on lung cancer treatment results are as follows: (1) The overall survival in the studied patient population is significantly lower with increasing distance to the oncology center; (2) The overall survival rate is significantly lower with increasing time required to reach the oncology center; (3) There is no correlation between metastatic stage at diagnosis and distance travelled; (4) There is no correlation between metastatic stage at diagnosis and travel time; (5) Male sex correlates with significantly increased risk of worse survival; (6) Age over ≥ 64 years correlates with an increased risk of worse survival; (7) As the clinical stage increases, overall survival decreases.

For the first time in national clinical oncology, such a comprehensive analysis of patients with lung cancer is carried out, focused on proving the role of distance and travel time to the oncology center as prognostic factors.

For the first time in Bulgaria, correlations are sought between clinical and pathological characteristics of patients with lung cancer and the distance and time to reach the oncology center. For the first time worldwide, a relationship between travel time and distance to the oncology center and survival of patients with histologically verified lung cancer is demonstrated using an analysis based on such a large patient cohort.

I believe that the distinguished contributions of the dissertant can be defined as having not only theoretical but also practical applicability. An innovative view of an often unrecognized factor of prognostic importance is presented, namely the patient's remoteness from the medical institution.

In connection with the dissertation, Dr. Teodorika Panayotova presents 6 publications in refereed international and national editions with impact factor.

The dissertation work is built clearly and thoroughly, sections have logical sequence. Good scientific language and free understanding of medical terminology are impressive.

The dissertation summary adequately reflects the content of the dissertation in a synthesized version.

Conclusion:

The dissertation of Dr. Teodorika Vitalinova Panayotova is a thorough, precisely conducted and presented scientific research.

The dissertation has up-to-date and scientific-applied value. The aim and objectives are precisely set, the results obtained are convincing, the conclusions are clearly formulated and comprehensive. The contributions have theoretical and practical value and outline guidelines for future research studies. The dissertation covers the quantitative indicators for acquiring the educational and scientific degree "Doctor" and fully meets the requirements of the Law for the development of the scientific staff in Republic of Bulgaria

In view of the above statements, I give a positive assessment of the dissertation of Dr. Teodorika Vitalinova Panayotova and recommend to the esteemed Scientific Jury to award her the scientific and educational degree "DOCTOR".

/Associate Professor Zhelyazko Arabadzhiev, MD, PhD/

