STATEMENT

From: Prof. Dr. Nikolay Vladimirov Conev, PhD

Clinic of Medical Oncology, UMHAT "Sveta Marina", Medical University - Varna

Chairman of the scientific jury, as per Order by the Rector of the Medical University - Varna.

Regarding the dissertation titled: "Prevalence of PIK3CA-mutations and response to first-line endocrine therapy in the population of Bulgarian patients with HR (+) HER2 (-) metastatic breast cancer"

Author: Dr. Radostina Bozhidarova Gencheva, PhD student at the Department of Oncology, Faculty of Medicine, Medical University – Varna.

Procedure: For awarding the educational and scientific degree of "Doctor" (PhD) in the scientific specialty "Oncology" (code 03.01.46).

Scientific Supervisor: Assoc. Prof. Eleonora Georgieva Dimitrova-Gospodinova, PhD.

1. General Overview of the Procedure and the Doctoral Candidate

The submitted set of documents complies with the requirements of the Development of Academic Staff in the Republic of Bulgaria Act (ZRASRB) and the Regulations of MU-Varna. Dr. Radostina Gencheva graduated in Medicine from MU-Sofia in 2008. Since 2018, she has been working as a resident at the Oncology Clinic of "Nadezhda" Hospital. She possesses solid professional training, and her dissertation is the result of in-depth research in the field of metastatic breast cancer.

2. Relevance of the Topic

Breast cancer is the leading oncological disease among women worldwide and in Bulgaria. The topic of the dissertation is highly relevant, as PIK3CA mutations are a key factor in endocrine

resistance. Investigating their prevalence and impact on therapeutic response within the Bulgarian population is of great importance for refining therapeutic approaches and implementing personalized medicine.

3. Characteristics and Evaluation of the Dissertation

The work consists of 115 pages and follows a classical structure:

Structure: Includes an introduction, aims and objectives, materials and methods, results, discussion, conclusions, and contributions.

Illustrative material: Contains 6 tables and 29 figures, which clearly present the obtained data.

Bibliography: 266 literary sources are cited, all in Latin script, demonstrating an excellent command of the current state of the problem.

4. Research Methodology

The study included 250 patients, with 250 paraffin blocks analyzed for the presence of PIK3CA mutations. Modern genetic and statistical methods were employed, ensuring high reliability of the results.

5. Scientific Results and Contributions

The main contributions of the dissertation are of a scientific and applied nature:

- For the first time, the prevalence of PIK3CA mutations has been established specifically within the Bulgarian population of patients with metastatic breast cancer.
- It has been proven that there is no significant difference in the frequency of the mutation in Bulgaria compared to global data.
- It was established that mutational status does not directly correlate with core clinical-pathological characteristics such as age and type of metastases, highlighting the need for genetic testing regardless of the clinical presentation.

6. Publications and Scientific Activity

In connection with the dissertation, 5 scientific publications and participations in prestigious forums have been presented. Of particular significance is the article in the journal Cancer Reports (2024), as well as the abstract presented at the ASCO Annual Meeting (2023). Dr. Gencheva is the lead author in most of them, which proves her personal contribution.

Conclusion

The dissertation of Dr. Radostina Gencheva is a contemporary and thorough study with significant scientific and practical value for oncology. The work fully meets the requirements of the ZRASRB and the Regulations of MU-Varna.

Based on the above, I give my positive evaluation and recommend that the scientific jury award Dr. Radostina Bozhidarova Gencheva the educational and scientific degree of "Doctor" (PhD) in the scientific specialty "Oncology".

09. APR. 2026

VARNA

Заличено на основание чл. 5, §1, б. „В“ от Регламент (ЕС) 2016/679